

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 3 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-568 (CANCELED).

Claim 569 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a nucleic acid of interest;

providing or generating detectable non-radioactive nucleic acid fragments, each fragment comprising: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof, and (b) one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof;

subjecting said fragments to a sequencing gel to separate or resolve said fragments;

detecting non-radioactively the presence of each of said separated or resolved fragments by detecting the modified or labeled nucleotides or the modified or labeled nucleotide analogs that are incorporated within, or onto a terminus of, said fragments; and

determining the sequence of said nucleic acid of interest.

Claim 570 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said nucleic acid sequence of interest is derived from an organism.

Claim 571 (PREVIOUSLY PRESENTED) The process according to claim 570, wherein said organism comprises bacteria, fungi, viruses, yeast or mammals.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 4 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 572 (CANCELED).

Claim 573 (PREVIOUSLY PRESENTED) The process according to claim 571, wherein said mammals comprise human beings.

Claim 574 (PREVIOUSLY PRESENTED) The process according to claim 570, wherein said organism is living.

Claim 575 (PREVIOUSLY PRESENTED) The process according to claims 570 or 574, wherein said organism comprises prokaryotes or eukaryotes.

Claim 576 (CANCELED).

Claim 577 (PREVIOUSLY PRESENTED) The process according to claim 575, wherein said eukaryotic nucleic acid sequence of interest comprises a mammalian nucleic acid sequence contained within a chromosome.

Claims 578-581 (CANCELED).

Claim 582 (PREVIOUSLY PRESENTED) The process according to claim 577, wherein said mammalian chromosomal nucleic acid sequence comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 583 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said modified or labeled nucleotides or said modified or labeled nucleotide analogs are incorporated within, or onto a terminus of, said fragments with an enzyme.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 5 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 584 (PREVIOUSLY PRESENTED) The process according to claim 583, wherein said modified or labeled nucleotides or said modified or labeled nucleotide analogs comprise nucleoside triphosphates which comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, or a combination of any of the foregoing.

Claim 585 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Claim 586 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein the detectable non-radioactive nucleic acid fragments hybridize to the nucleic acid of interest or to a portion thereof prior to separation in said sequencing gel.

Claim 587 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein before or during said providing or generating step, at least one of the modified or labeled nucleotides or the modified or labeled nucleotide analogs are incorporated at a terminus of at least one of said fragments.

Claim 588 (PREVIOUSLY PRESENTED) The process according to claim 583, wherein at least one of said modified or labeled nucleotides or said modified or labeled nucleotide analogs is incorporated by an enzyme at a terminus of at least one of said fragments.

Claim 589 (PREVIOUSLY PRESENTED) The process according to claim 588, wherein said enzyme comprises a terminal transferase, a ligase or a polymerase.

Claims 590-591 (CANCELED).

Claim 592 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein at least one of said modified or labeled nucleotides or said modified or labeled nucleotide analogs is incorporated onto a terminus of said fragments through chemical coupling.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 6 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 593 (PREVIOUSLY PRESENTED) The process according to claim 592, wherein said chemical coupling is carried out with carbodiimide or formaldehyde.

Claim 594 (PREVIOUSLY PRESENTED) The process according to claim 587, 588 or 592, wherein said terminus is a 3' terminus or a 5' terminus.

Claims 595-596 (CANCELED).

Claim 597 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 598 (PREVIOUSLY PRESENTED) The process according to claim 597, wherein said polymerizing enzyme comprises a polymerase.

Claim 599 (PREVIOUSLY PRESENTED) The process according to claim 598, wherein said polymerase comprises DNA polymerase or RNA polymerase.

Enz-5(D8)(C2)

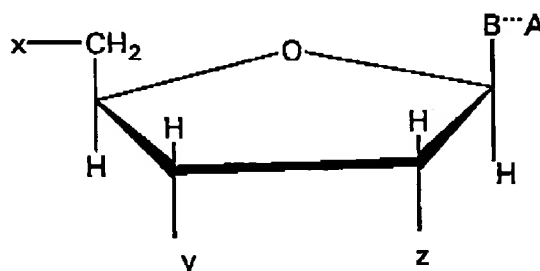
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 7 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 600 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein at said providing or generating step, the modified or labeled nucleotides or the modified or labeled nucleotide analogs comprise one or more structures which comprise:

- (i) a nucleotide structure or nucleotide analog structure having the formula



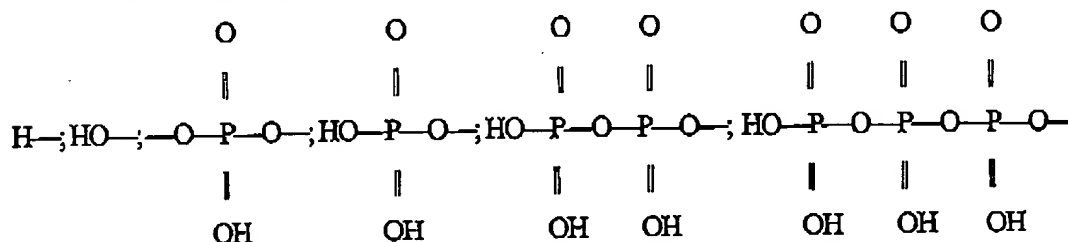
wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

wherein B and A are covalently attached directly or through a linkage group;

and

wherein x comprises:



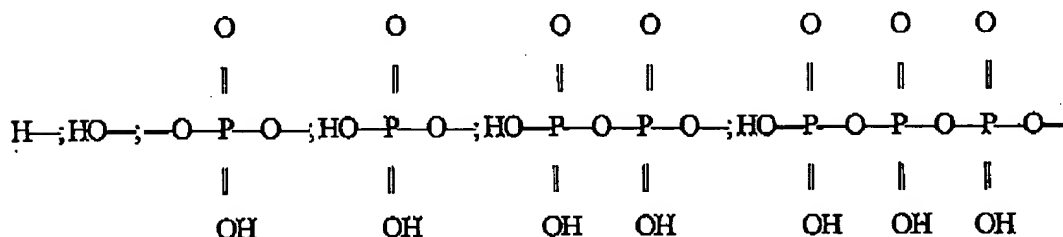
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 8 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

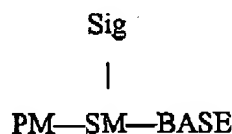
- September 19, 2005]

wherein y comprises:



wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

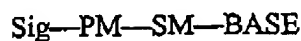
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 9 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
— September 19, 2005]

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 601 (CANCELED).

Claim 602 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (i), y and z are H—.

Claim 603 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein PM comprises a mono-phosphate, a di-phosphate, a tri-phosphate or a tetra-phosphate.

Claim 604 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claims 605-606 (CANCELED).

Claim 607 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein SM comprises ribose, deoxyribose or dideoxyribose.

Claim 608 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein B in said nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide structure or nucleotide analog structure (ii) or (iii) comprises a 7-deazapurine.

Claim 609 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 10 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 610 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (i), A is covalently attached to B at the C5 position, the C2 position, the N3 position, the C6 position, or combinations thereof when B is a pyrimidine, or is covalently attached to B at the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, or combinations thereof when B is a purine, or is covalently attached to B at the 7 position when the is a 7-deazapurine.

Claim 611 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein A in said nucleotide structure or nucleotide analog structure (i) is covalently attached to B at a position comprising the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, or combinations thereof.

Claim 612 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), PM is attached to SM at the 2', 3', 5' position, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 613 (CANCELED).

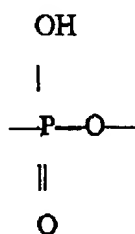
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

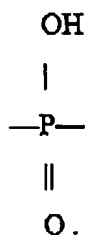
Page 11 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 614 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said covalent attachment in nucleotide structure or nucleotide analog structure (iii) comprises



or



Claim 615 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (iii) PM comprises a mono-, di- or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 616 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

Claim 617 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein, in nucleotide or nucleotide analog structure (i), said covalent attachment comprises a —CH₂NH— moiety, an olefinic bond at the α-position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or both.

Enz-5(D8)(C2)

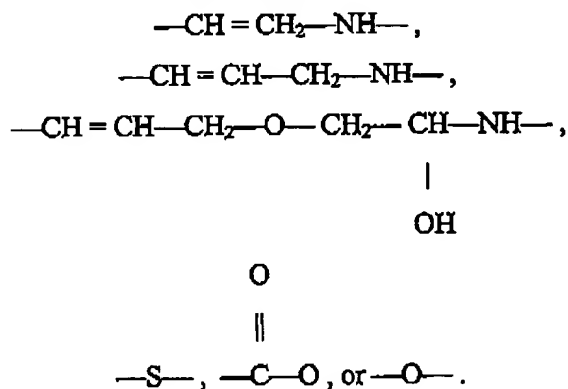
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 12 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 618 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 619 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or any of the moieties



Claim 620 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein, in nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises a glycosidic linkage moiety.

Claim 621 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein in said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B through a linkage group, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), said Sig is covalently attached to SM or PM through a linkage group.

Claim 622 (PREVIOUSLY PRESENTED) The process according to claim 621, wherein, in nucleotide or nucleotide analog structure (i), said linkage group comprises an amine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 13 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 623 (PREVIOUSLY PRESENTED) The process according to claim 622, wherein said amine comprises a primary amine.

Claim 624 (PREVIOUSLY PRESENTED) The process according to claim 621, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claims 625-633 (CANCELED).

Claim 634 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A comprises more than three carbon atoms or said Sig comprises at least three carbon atoms.

Claim 635 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A or said Sig comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 636 (CANCELED).

Claim 637 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A or said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety.

Claim 638 (PREVIOUSLY PRESENTED) The process according to claim 637, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claims 639-640 (CANCELED).

Claim 641 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A or said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 14 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 642 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A or said Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component chelating component or a combination of any of the foregoing.

Claims 643-645 (CANCELED).

Claim 646 (PREVIOUSLY PRESENTED) The process according to claim 642, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 647 (CANCELED).

Claim 648 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A or said Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 649 (PREVIOUSLY PRESENTED) The process according to claim 648, wherein the binding protein comprises a lectin.

Claim 650 (PREVIOUSLY PRESENTED) The process according to claim 649, wherein the lectin comprises concanavalin A.

Claim 651 (PREVIOUSLY PRESENTED) The process according to claim 649, wherein said lectin is conjugated to ferritin.

Claims 652-655 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 15 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 656 (PREVIOUSLY PRESENTED) The process according to claim 642, wherein said metal-containing component is catalytic.

Claim 657 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said A or said Sig is a non-radioactively detectable indicator molecule.

Claim 658 (PREVIOUSLY PRESENTED) The process according to claim 657, wherein said indicator molecule comprises an aromatic structure.

Claim 659 (PREVIOUSLY PRESENTED) The process according to claim 658, wherein said aromatic structure is heterocyclic.

Claim 660 (PREVIOUSLY PRESENTED). The process according to claim 659, wherein said heterocyclic aromatic structure is fluorescent.

Claim 661 (PREVIOUSLY PRESENTED) The process according to claim 660, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or a combination of any of the foregoing.

Claims 662-666 (CANCELED).

Claim 667 (PREVIOUSLY PRESENTED) The process according to claim 642, wherein said A or said Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claims 668-669 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 16 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 670 (PREVIOUSLY PRESENTED) The process according to claim 657, wherein said indicator molecule comprises a member comprising a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

Claims 671-706 (CANCELED).

Claim 707 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said detectable non-radioactive nucleic acid fragments are detectable by a non-radioactive means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 708 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said subjecting step is carried out electrophoretically.

Claim 709 (PREVIOUSLY PRESENTED) The process according to claims 569 or 600, wherein said detecting step is carried out directly.

Claim 710 (PREVIOUSLY PRESENTED) The process according to claim 709, wherein the detectable non-radioactive fragments comprise one or more non-radioactively detectable indicator molecules and said direct detection is carried out using these indicator molecules.

Claim 711 (PREVIOUSLY PRESENTED) The process according to claim 710, wherein said non-radioactively detectable indicator molecules comprise fluorescently labeled nucleotides.

Claim 712 (PREVIOUSLY PRESENTED) The process according to claim 711, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 713 (PREVIOUSLY PRESENTED) The process according to claim 709, wherein said detecting step is carried out by means of a directly detectable signal provided by said modified or labeled nucleotides or modified or labeled nucleotide analogs, A or Sig.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 17 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 714 (PREVIOUSLY PRESENTED) The process according to claim 713, wherein in said detecting step the directly detectable signal comprises a chelating structure, a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Claim 715 (CANCELED).

Claim 716 (PREVIOUSLY PRESENTED) The process according to claim 600, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said modified or labeled nucleotides or modified or labeled nucleotide analogs, A or Sig .

Claim 717 (PREVIOUSLY PRESENTED) The process according to claim 716, wherein in said detecting step the indirectly detectable signal comprises an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 718 (CANCELED).

Claim 719 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs are capable of being detected non-radioactively by a member comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 720 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said detecting step comprises localizing said non-radioactively labeled nucleic acid fragments by means of said detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 18 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 721 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a nucleic acid of interest;

providing or generating detectable non-radioactive nucleic acid fragments that are non-radioactively labeled, each fragment comprising: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof, and (b) one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof;

introducing or subjecting said fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel;

detecting non-radioactively each of the separated or resolved fragments; and

determining the sequence of said nucleic acid of interest.

Claim 722 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 723 (PREVIOUSLY PRESENTED) The process according to claim 722, wherein said organism comprises bacteria, fungi, viruses, yeast, or mammals.

Claim 724 (CANCELED).

Claim 725 (PREVIOUSLY PRESENTED) The process according to claim 723, wherein said mammals comprise human beings.

Claim 726 (PREVIOUSLY PRESENTED) The process according to claim 722, wherein said organism is living.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 19 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 727 (PREVIOUSLY PRESENTED) The process according to claims 722 or 726, wherein said organism comprises prokaryotes or eukaryotes.

Claim 728 (CANCELED).

Claim 729 (PREVIOUSLY PRESENTED) The process according to claim 727, wherein said eukaryotic nucleic acid sequence of interest comprises a mammalian nucleic acid sequence contained within a chromosome.

Claims 730-733 (CANCELED).

Claim 734 (PREVIOUSLY PRESENTED) The process according to claim 729, wherein said mammalian chromosomal nucleic acid sequence comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 735 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein in said providing or generating step the fragments are provided or generated by one or more primers, nucleoside triphosphates, or a combination thereof.

Claim 736 (PREVIOUSLY PRESENTED) The process according to claim 735, wherein said nucleoside triphosphates comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, or a combination of any of the foregoing.

Claim 737 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 20 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 738 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein the detectable non-radioactively labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

Claim 739 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein at said providing or generating step, the modified or labeled nucleotides or modified or labeled nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

Claim 740 (PREVIOUSLY PRESENTED) The process according to claim 739, wherein at least one of said modified or labeled nucleotides or modified or labeled nucleotide analogs is at a terminus of at least one of said fragments.

Claim 741 (PREVIOUSLY PRESENTED) The process according to claim 740, wherein said terminus comprises the 5' or the 3' terminus.

Claim 742 (PREVIOUSLY PRESENTED) The process according to claim 739, wherein said incorporation has been carried out in the presence of a primer.

Claim 743 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said nucleotide analog can be attached terminally to DNA or RNA by means of an enzyme.

Claim 744 (PREVIOUSLY PRESENTED) The process according to claim 743, wherein said enzyme comprises terminal transferase, a ligase or a polymerase.

Claim 745 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said nucleotide analog has been coupled to DNA or RNA by a coupling means comprising chemical coupling or enzymatic coupling.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 21 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 746 (PREVIOUSLY PRESENTED) The process according to claim 745, wherein said chemical coupling can be carried out by a chemical coupling means comprising carbodiimide or formaldehyde.

Claim 747 (PREVIOUSLY PRESENTED) The process according to claim 745, wherein said enzymatic coupling can be carried out by an enzymatic coupling means comprising DNA ligase or RNA ligase.

Claim 748 (CANCELED).

Claim 749 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 750 (PREVIOUSLY PRESENTED) The process according to claim 749, wherein said polymerizing enzyme comprises a polymerase.

Claim 751 (PREVIOUSLY PRESENTED) The process according to claim 750, wherein said polymerase comprises DNA polymerase or RNA polymerase.

Claim 752 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein at said providing or generating step, the modified or labeled nucleotides or the modified or labeled nucleotide analogs comprise one or more structures which comprise:

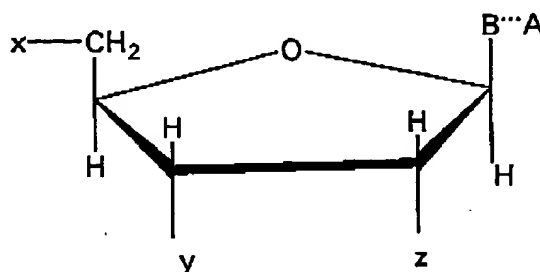
- (i) a nucleotide structure or nucleotide analog structure having the formula

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 22 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

- September 19, 2005]



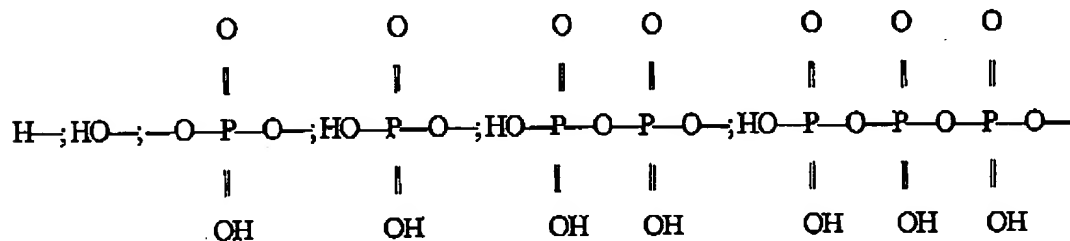
wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

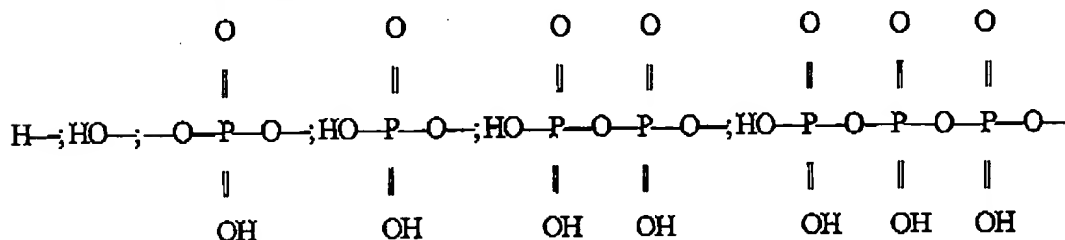
wherein B and A are covalently attached directly or through a linkage group;

and

wherein x comprises:



wherein y comprises:



Enz-5(D8)(C2)

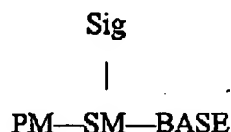
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 23 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

wherein z comprises H— or HO—;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

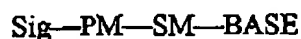
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 24 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
— September 19, 2005]

Claim 753 (CANCELED).

Claim 754 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein in said nucleotide structure or nucleotide analog structure (i), y and z are H—.

Claim 755 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein PM comprises a mono-phosphate, a di-phosphate, a tri-phosphate or a tetra-phosphate.

Claim 756 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claims 757-758 (CANCELED).

Claim 759 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein SM comprises ribose, 2'-deoxyribose, 3'-deoxyribose or 2', 3'- dideoxyribose.

Claim 760 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein B in said nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide structure or nucleotide analog structure (ii) or (iii) comprises a 7-deazapurine.

Claim 761 (CANCELED).

Claim 762 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein A in said nucleotide or nucleotide analog structure (i) is covalently attached to the C5 position, the C2 position, the N3 position, the C6 position, or combinations thereof when B is a pyrimidine, or is covalently attached to the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, or combinations thereof when B is a purine, or is covalently attached to B at the 7-position when B is a 7-deazapurine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 25 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

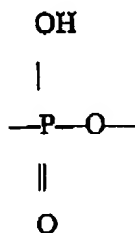
— September 19, 2005]

Claim 763 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein A in said nucleotide or nucleotide analog structure (i) is covalently attached to B at a position comprising the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, or combinations thereof.

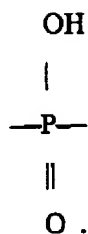
Claim 764 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein in said nucleotide or nucleotide analog structure (ii) or (iii), PM is attached to SM at the 2', 3', 5' position, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 765 (CANCELED).

Claim 766 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said covalent attachment in nucleotide or nucleotide analog structure (iii) comprises:



or



Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 26 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 767 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein in said nucleotide structure or nucleotide analog structure (iii) PM comprises a mono-, di or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 768 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

Claim 769 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises a —CH₂NH— moiety, an olefinic bond at the α -position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i), or both.

Claim 770 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein, in said nucleotide or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

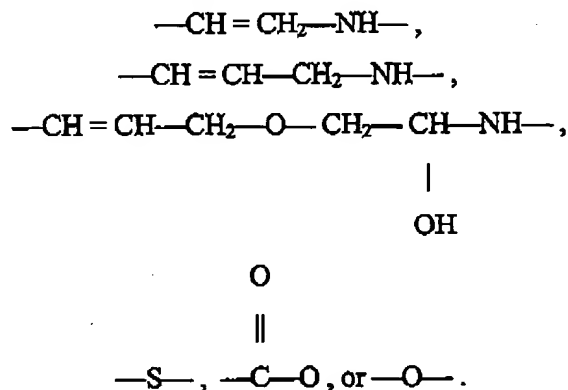
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 27 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 771 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises an olefinic bond at the α -position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i), or any of the moieties



Claim 772 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises a glycosidic linkage moiety.

Claim 773 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein in said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii) said Sig is covalently attached to SM or PM through a linkage group.

Claim 774 (PREVIOUSLY PRESENTED) The process according to claim 773, wherein, in said nucleotide structure or nucleotide analog structure (i), said linkage group comprises an amine.

Claim 775 (PREVIOUSLY PRESENTED) The process according to claim 774, wherein said amine comprises a primary amine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 28 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 776 (PREVIOUSLY PRESENTED) The process according to claim 773, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claims 777-785 (CANCELED).

Claim 786 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A comprises more than three carbon atoms and Sig comprises at least three carbon atoms.

Claim 787 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A or said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 788 (CANCELED).

Claim 789 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A or said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety.

Claim 790 (PREVIOUSLY PRESENTED) The process according to claim 789, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claims 791-792 (CANCELED).

Claim 793 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A or said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 29 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 794 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A or said Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component a chelating component, or any combination of the foregoing.

Claim 795 (CANCELED).

Claim 796 (PREVIOUSLY PRESENTED) The process according to claim 794, wherein said electron dense component comprises ferritin.

Claim 797 (PREVIOUSLY PRESENTED) The process according to claim 794, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claims 798-799 (CANCELED).

Claim 800 (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A or said Sig comprises a sugar residue and said sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 801 (PREVIOUSLY PRESENTED) The process according to claim 800, wherein the binding protein comprises a lectin.

Claim 802 (PREVIOUSLY PRESENTED) The process according to claim 801, wherein the lectin comprises concanavalin A.

Claim 803 (PREVIOUSLY PRESENTED) The process according to claim 801, wherein said lectin is conjugated to ferritin.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 30 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claims 804-807 (CANCELED).

Claim 808 (PREVIOUSLY PRESENTED) The process according to claim 794, wherein said metal-containing component is catalytic.

Claim 809. (PREVIOUSLY PRESENTED) The process according to claim 752, wherein said A or said Sig is a non-radioactively detectable indicator molecule.

Claim 810 (PREVIOUSLY PRESENTED) The process according to claim 809, wherein said indicator molecule comprises an aromatic structure.

Claim 811 (PREVIOUSLY PRESENTED) The process according to claim 810, wherein said aromatic structure is heterocyclic.

Claim 812 (PREVIOUSLY PRESENTED) The process according to claim 811, wherein said heterocyclic aromatic structure is fluorescent.

Claim 813 (PREVIOUSLY PRESENTED) The process according to claim 812, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or a combination of any of the foregoing.

Claims 814-818 (CANCELED).

Claim 819 (PREVIOUSLY PRESENTED) The process according to claim 794, wherein said A or said Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claims 820-821 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 31 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)]

- September 19, 2005]

Claim 822 (PREVIOUSLY PRESENTED) The process according to claim 809, wherein said indicator molecule comprises a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

Claims 823-858 (CANCELED).

Claim 859 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said detectable non-radioactively labeled nucleic acid fragments are detectable by a non-radioactive means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 860 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said separating or resolving step is carried out electrophoretically.

Claim 861 (PREVIOUSLY PRESENTED) The process according to claims 721 or 752, wherein said detecting step is carried out directly.

Claim 862 (PREVIOUSLY PRESENTED) The process according to claim 861, wherein the detectable non-radioactive fragments comprise one or more non-radioactively detectable indicator molecules and said direct detection is carried out using these indicator molecules.

Claim 863 (PREVIOUSLY PRESENTED) The process according to claim 862, wherein said non-radioactively detectable indicator molecules comprise fluorescently labeled nucleotides.

Claim 864 (PREVIOUSLY PRESENTED) The process according to claim 863, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 32 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)]

– September 19, 2005]

Claim 865 (PREVIOUSLY PRESENTED) The process according to claim 861, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more modified or labeled nucleotides or modified or labeled nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 866 (PREVIOUSLY PRESENTED) The process according to claim 865, wherein in said detecting step the directly detectable signal comprises a chelating structure, a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Claim 867 (CANCELED).

Claim 868 (PREVIOUSLY PRESENTED) The process according to claims 721 or 752, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said one or more non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 869 (PREVIOUSLY PRESENTED) The process according to claim 868, wherein in said detecting step the indirectly detectable signal comprises an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 870 (CANCELED).

Claim 871 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said one or more modified or labeled nucleotides or modified or labeled nucleotide analogs are capable of being detected by means comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 33 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)]

- September 19, 2005]

Claim 872 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 873 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a nucleic acid of interest;

providing or generating detectable non-radioactive nucleic acid fragments that are non-radioactively labeled, each fragment comprising : (a) a sequence complementary to said nucleic acid of interest or to a portion thereof and (b) one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA;

detecting non-radioactively the detectable non-radioactive labeled nucleic acid fragments with a sequencing gel; and

determining the sequence of said nucleic acid of interest.

Claim 874 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 875 (PREVIOUSLY PRESENTED) The process according to claim 874, wherein said organism comprises bacteria, fungi, viruses, yeast, or mammals.

Claim 876 (CANCELED).

Claim 877 (PREVIOUSLY PRESENTED) The process according to claim 875, wherein said mammals comprise human beings.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 34 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)]

– September 19, 2005]

Claim 878 (PREVIOUSLY PRESENTED) The process according to claim 874, wherein said organism is living.

Claim 879 (PREVIOUSLY PRESENTED) The process according to claims 874 or 878, wherein said organism comprises prokaryotes or eukaryotes.

Claim 880 (CANCELED).

Claim 881 (PREVIOUSLY PRESENTED) The process according to claim 879, wherein said eukaryotic nucleic acid sequence of interest comprises a mammalian nucleic acid sequence contained within a chromosome.

Claims 882-885 (CANCELED).

Claim 886 (PREVIOUSLY PRESENTED) The process according to claim 881, wherein said mammalian chromosomal nucleic acid sequence comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 887 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein in said providing or generating step, the fragments are provided or generated by one or more primers, nucleoside triphosphates, or a combination thereof.

Claim 888 (PREVIOUSLY PRESENTED) The process according to claim 887, wherein said nucleoside triphosphates comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, or a combination of any of the foregoing.

Claim 889 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 35 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 890 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented and separated prior to detecting in said sequencing gel.

Claim 891. (PREVIOUSLY PRESENTED) The process according to claim 873, wherein in said providing or generating step, the one or more modified or labeled nucleotides or modified or labeled nucleotide analogs have been incorporated into said nucleic acid fragment or fragments.

Claim 892 (PREVIOUSLY PRESENTED) The process according to claim 891, wherein at least one of said modified or labeled nucleotides or modified or labeled nucleotide analogs is at a terminus of at least one of said fragment or fragments.

Claim 893 (PREVIOUSLY PRESENTED) The process according to claim 892, wherein said terminus comprises the 5' or the 3' terminus.

Claim 894 (PREVIOUSLY PRESENTED) The process according to claim 891, wherein said incorporation has been carried out in the presence of a primer.

Claim 895 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said modified or labeled nucleotide or modified or labeled nucleotide analog has been attached terminally to DNA or RNA by means of an enzyme.

Claim 896. (PREVIOUSLY PRESENTED) The process according to claim 895, wherein said enzyme comprises terminal transferase, a ligase or a polymerase.

Claim 897 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said nucleotide analog has been coupled to DNA or RNA by a coupling means comprising chemical coupling or enzymatic coupling.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 36 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 898 (PREVIOUSLY PRESENTED) The process according to claim 897, wherein said chemical coupling has been carried out by a chemical coupling means comprising carbodiimide or formaldehyde.

Claim 899 (PREVIOUSLY PRESENTED) The process according to claim 898, wherein said enzymatic coupling has been carried out by an enzymatic coupling means comprising DNA ligase or RNA ligase.

Claim 900 (CANCELED).

Claim 901 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 902 (PREVIOUSLY PRESENTED) The process according to claim 901, wherein said polymerizing enzyme comprises a polymerase and the modified or labeled nucleotide or modified or labeled nucleotide analog is incorporated at a 3' terminus.

Claim 903 (PREVIOUSLY PRESENTED) The process according to claim 902, wherein said polymerizing enzyme comprises DNA polymerase or RNA polymerase.

Claim 904 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein in said providing or generating step, the non-radioactive modified or labeled nucleotides or the modified or labeled nucleotide analogs comprise one or more structures which comprise:

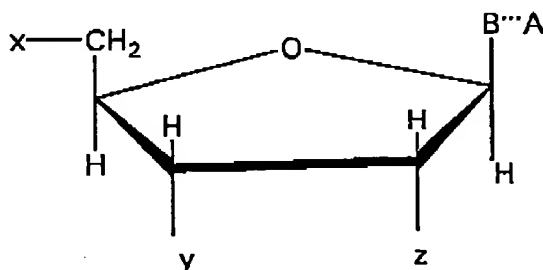
- (i) a nucleotide structure or nucleotide analog structure having the formula

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 37 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)]

– September 19, 2005]



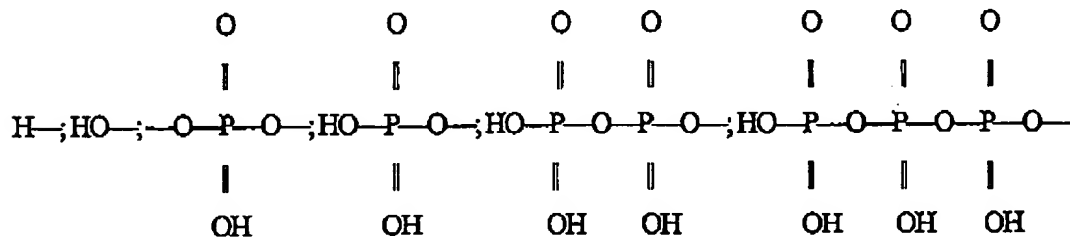
wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

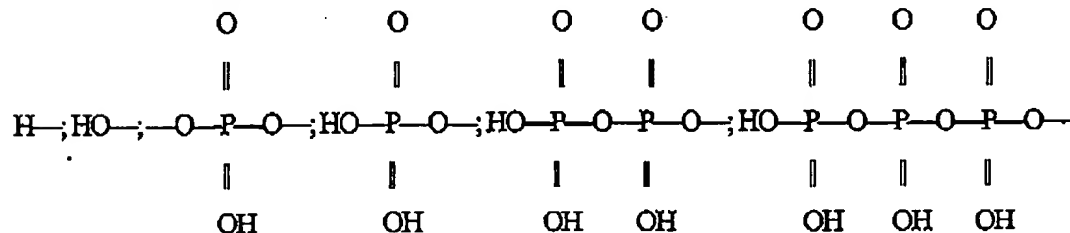
wherein B and A are covalently attached directly or through a linkage group;

and

wherein x comprises:



wherein y comprises:

**Enz-5(D8)(C2)**

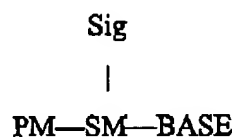
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 38 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

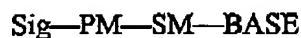
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 905 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 39 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 906 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein in said nucleotide structure or nucleotide analog structure (i), y and z are H—.

Claim 907 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein PM comprises a mono-phosphate, a di-phosphate, a tri-phosphate or a tetra-phosphate.

Claim 908 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claims 909-910 (CANCELED).

Claim 911 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein SM comprises ribose, 2'-deoxyribose, 3'-deoxyribose or 2', 3'-dideoxyribose.

Claim 912 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein B in said nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide structures (ii) or (iii) comprises a 7-deazapurine.

Claim 913 (CANCELED).

Claim 914 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein A in said nucleotide structure or nucleotide analog structure (i) is covalently attached to the C5 position, the C2 position, the N3 position, the C6 position, or combinations thereof when B is a pyrimidine, or is covalently attached to the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, or combinations thereof when B is a purine, or is covalently attached to the 7-position when B is a 7-deazapurine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 40 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

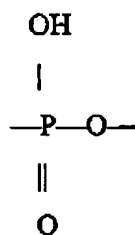
— September 19, 2005]

Claim 915 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein A in said nucleotide structure or nucleotide analog structure (i) is covalently attached to B at a position comprising the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, or combinations thereof.

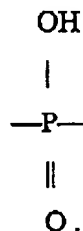
Claim 916 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), PM is attached to SM at the 2', 3', 5' position, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 917 (CANCELED).

Claim 918 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said covalent attachment in nucleotide structure or nucleotide analog structure (iii) comprises



or



Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 41 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 919 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein in said nucleotide structure or nucleotide analog structure PM comprises a mono-, di- or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 920 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

Claim 921 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein, in nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises: a —CH₂NH— moiety, an olefinic bond at the α -position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i), or both.

Claim 922 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

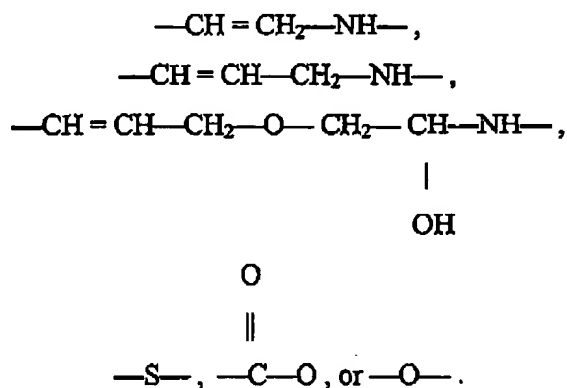
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 42 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 923 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide structure (i), or any of the moieties



Claim 924 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises a glycosidic linkage moiety.

Claim 925 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein in said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii) said Sig is covalently attached to SM or PM through a linkage group.

Claim 926 (PREVIOUSLY PRESENTED) The process according to claim 925, wherein, in nucleotide structure (i), said linkage group comprises an amine.

Claim 927 (PREVIOUSLY PRESENTED) The process according to claim 926, wherein said amine comprises a primary amine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 43 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 928 (PREVIOUSLY PRESENTED) The process according to claim 925, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claims 929-937 (CANCELED).

Claim 938 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A comprises more than three carbon atoms and Sig comprises at least three carbon atoms.

Claim 939 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A or said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 940 (CANCELED).

Claim 941 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A or said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety.

Claim 942 (PREVIOUSLY PRESENTED) The process according to claim 941, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claims 943-944 (CANCELED).

Claim 945 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A or said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 44 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 946 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A or said Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or any combination of any of the foregoing.

Claim 947 (PREVIOUSLY PRESENTED) The process according to claim 946, wherein said electron dense component comprises ferritin.

Claim 948 (CANCELED).

Claim 949 (PREVIOUSLY PRESENTED) The process according to claim 946, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claims 950-951 (CANCELED).

Claim 952 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A or said Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 953 (PREVIOUSLY PRESENTED) The process according to claim 952, wherein the binding protein comprises a lectin.

Claim 954 (PREVIOUSLY PRESENTED) The process according to claim 953, wherein the lectin comprises concanavalin A.

Claim 955 (PREVIOUSLY PRESENTED) The process according to claim 953, wherein said lectin is conjugated to ferritin.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 45 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claims 956-959 (CANCELED).

Claim 960 (PREVIOUSLY PRESENTED) The process according to claim 946, wherein said metal-containing component is catalytic.

Claim 961 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein said A or said Sig is a non-radioactively detectable indicator molecule.

Claim 962 (PREVIOUSLY PRESENTED) The process according to claim 961, wherein said indicator molecule comprises an aromatic structure.

Claim 963 (PREVIOUSLY PRESENTED) The process according to claim 962, wherein said aromatic structure is heterocyclic.

Claim 964 (PREVIOUSLY PRESENTED) The process according to claim 963, wherein said heterocyclic aromatic structure is fluorescent.

Claim 965 (PREVIOUSLY PRESENTED) The process according to claim 904, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or a combination of any of the foregoing.

Claims 966-970 (CANCELED).

Claim 971 (PREVIOUSLY PRESENTED) The process according to claim 946, wherein said A or said Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claims 972-973 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 46 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 974 (PREVIOUSLY PRESENTED) The process according to claim 961, wherein said indicator molecule comprises a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

Claims 975-1010 (CANCELED).

Claim 1011 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said detectable non-radioactive labeled nucleic acid fragments are detectable by a non-radioactive means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1012 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

Claim 1013 (PREVIOUSLY PRESENTED) The process according to claims 873 or 904, wherein said detecting step is carried out directly.

Claim 1014 (PREVIOUSLY PRESENTED) The process according to claim 1013, wherein the detectable non-radioactive fragments comprise one or more non-radioactively detectable indicator molecules and said direct detection is carried out using one or more of these indicator molecules.

Claim 1015 (PREVIOUSLY PRESENTED) The process according to claim 1014, wherein said one or more non-radioactively detectable indicator molecule comprises fluorescently labeled nucleotides.

Claim 1016 (PREVIOUSLY PRESENTED) The process according to claim 1015, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 47 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1017 (PREVIOUSLY PRESENTED) The process according to claim 1016, wherein said detecting step is carried out by means of a directly detectable signal provided by said A, Sig or modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1018 (PREVIOUSLY PRESENTED) The process according to claim 1013, wherein in said detecting step the directly detectable signal comprises a chelating structure, a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Claim 1019 (CANCELED).

Claim 1020 (PREVIOUSLY PRESENTED) The process according to claims 873 or 904, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said A, Sig or modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1021 (PREVIOUSLY PRESENTED) The process according to claim 1020, wherein in said detecting step the indirectly detectable signal comprises an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 1022 (CANCELED).

Claim 1023 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs are capable of being detected by means comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1024 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said modified or labeled nucleotides or modified or labeled nucleotide analogs.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 48 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1025 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising detecting non-radioactively one or more detectable non-radioactive labeled nucleic acid fragments which have been resolved or separated by a sequencing gel, wherein each of said fragments comprises: (a) a sequence complementary to said nucleic acid of interest or to a portion thereof; and (b) one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof.

Claim 1026 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 1027 (PREVIOUSLY PRESENTED) The process according to claim 1026, wherein said organism comprises bacteria, fungi, viruses, yeast or mammals.

Claim 1028 (CANCELED).

Claim 1029 (PREVIOUSLY PRESENTED) The process according to claim 1027, wherein said mammals comprise human beings.

Claim 1030 (PREVIOUSLY PRESENTED) The process according to claim 1026, wherein said organism is living.

Claim 1031 (PREVIOUSLY PRESENTED) The process according to claims 1026 or 1030, wherein said organism comprises prokaryotes or eukaryotes.

Claim 1032 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 49 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1033 (PREVIOUSLY PRESENTED) The process according to claim 1031, wherein said eukaryotic nucleic acid sequence of interest comprises a mammalian nucleic acid sequence contained within a chromosome.

Claims 1034-1037 (CANCELED).

Claim 1038 (PREVIOUSLY PRESENTED) The process according to claim 1033, wherein said mammalian chromosomal nucleic acid sequence comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 1039 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein prior to said detecting step, the fragments are provided or generated by one or more primers or nucleoside triphosphates, or a combination thereof.

Claim 1040 (PREVIOUSLY PRESENTED) The process according to claim 1039, wherein said nucleoside triphosphates comprise ribonucleoside triphosphates, deoxyribonucleoside triphosphates, dideoxyribonucleoside triphosphates, or a combination of any of the foregoing.

Claim 1041 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said fragments have been obtained or generated by a nucleic acid sequencing step or technique.

Claim 1042 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein the detectable non-radioactive labeled complementary nucleic acid is fragmented prior to separation in said sequencing gel.

Claim 1043 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein prior to said detecting step, the modified or labeled nucleotides or modified or labeled nucleotide analogs have been incorporated into said fragments.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 50 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1044 (PREVIOUSLY PRESENTED) The process according to claim 1043, wherein at least one of said modified or labeled nucleotides or modified or labeled nucleotide analogs is at a terminus of at least one of said fragments.

Claim 1045 (PREVIOUSLY PRESENTED) The process according to claim 1044, wherein said terminus comprises the 5' or the 3' terminus.

Claim 1046 (PREVIOUSLY PRESENTED) The process according to claim 1043, wherein said incorporation has been carried out in the presence of a primer.

Claim 1047 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said modified or labeled nucleotide or modified or labeled nucleotide analog has been attached terminally to DNA or RNA by means of an enzyme.

Claim 1048 (PREVIOUSLY PRESENTED) The process according to claim 1047, wherein said enzyme comprises terminal transferase, a ligase or a polymerase.

Claim 1049 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said nucleotide analog has been coupled to DNA or RNA by a coupling means comprising chemical coupling or enzymatic coupling.

Claim 1050 (PREVIOUSLY PRESENTED) The process according to claim 1049, wherein said chemical coupling has been carried out by a chemical coupling means comprising carbodiimide or formaldehyde.

Claim 1051 (PREVIOUSLY PRESENTED) The process according to claim 1049, wherein said incorporation is carried out by a DNA ligase or RNA ligase.

Claim 1052 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 51 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

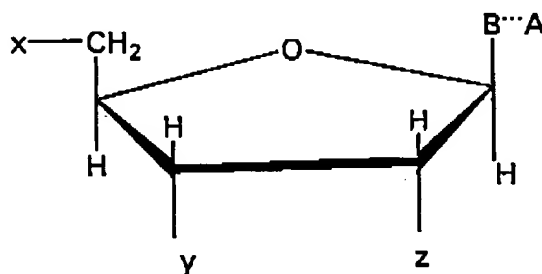
Claim 1053 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 1054 (PREVIOUSLY PRESENTED) The process according to claim 1053, wherein said polymerizing enzyme comprises a polymerase and the modified or labeled nucleotide or modified or labeled nucleotide analog is incorporated at a 3' terminus.

Claim 1055 (PREVIOUSLY PRESENTED) The process according to claim 1054, wherein said polymerase comprises DNA polymerase or RNA polymerase.

Claim 1056 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein in said detecting step, the modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more structures:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein B comprises a purine moiety, a 7-deazapurine moiety or a pyrimidine moiety, and B is covalently bonded to the C1' position of the furanosyl moiety, provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 52 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

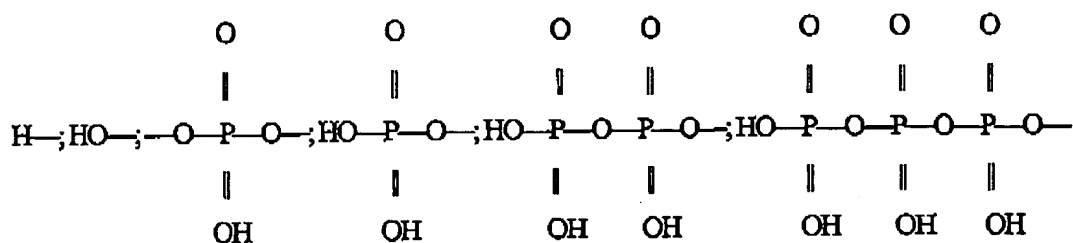
- September 19, 2005]

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal;

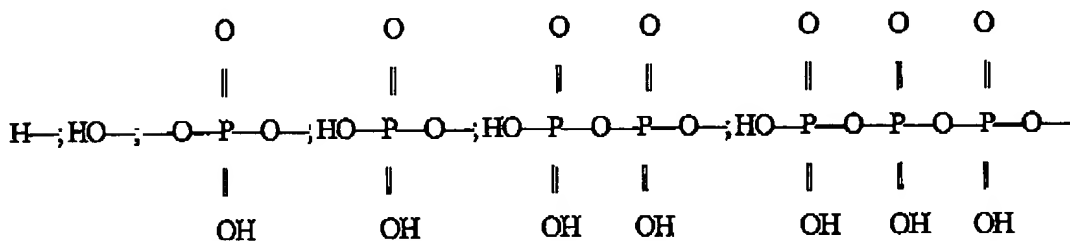
wherein B and A are covalently attached directly or through a linkage group;

and

wherein x comprises:

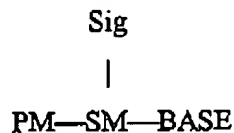


wherein y comprises:



wherein z comprises H- or HO-;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 53 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

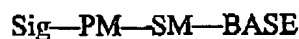
— September 19, 2005]

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group.

Claim 1057 (CANCELED).

Claim 1058 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein in said nucleotide structure or nucleotide analog structure (i) y and z are H—.

Claim 1059 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein PM comprises a mono-phosphate, a di-phosphate, a tri-phosphate or a tetra-phosphate.

Claim 1060 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 54 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claims 1061-1062 (CANCELED).

Claim 1063 (PREVIOUSLY PRESENTED) The process according to claim 1025 or 1056 ,
wherein SM comprises ribose, 2'-deoxyribose, 3'-deoxyribose or 2', 3'-dideoxyribose.

Claim 1064 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein B in
said nucleotide structure or nucleotide analog structure (i) or BASE in any of said nucleotide or
nucleotide analog structure (ii) or (iii) comprises a 7-deazapurine.

Claim 1065 (CANCELED).

Claim 1066 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein in said
nucleotide structure or nucleotide analog structure (i), A is covalently attached to the C5 position,
the C2 position, the N3 position, the C6 position, or combinations thereof when B is a pyrimidine,
or is covalently attached to the C8 position, the N1 position, the C2 position, the N3 position, the C6
position, the N7 position, or combinations thereof when B is a purine, or is covalently attached to B
the at a 7-position when B is a 7-deazapurine.

Claim 1067 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein A in
said nucleotide or nucleotide analog structure (i) is covalently attached to B at a position comprising
the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine
comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or
deazaguanine, or combinations thereof.

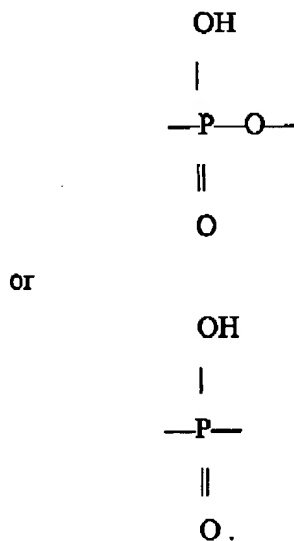
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
 Page 55 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
 (Following The September 8, 2005 Advisory Action)
 – September 19, 2005]

Claim 1068 (PREVIOUSLY PRESENTED) The process according to claim 1062, wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), PM is attached to SM at a position independently comprising the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1069 (CANCELED).

Claim 1070 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said covalent attachment in nucleotide structure or nucleotide analog structure (iii) comprises



Claim 1071 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein in said nucleotide structure or nucleotide analog structure (iii) PM comprises a mono-, di or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 56 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

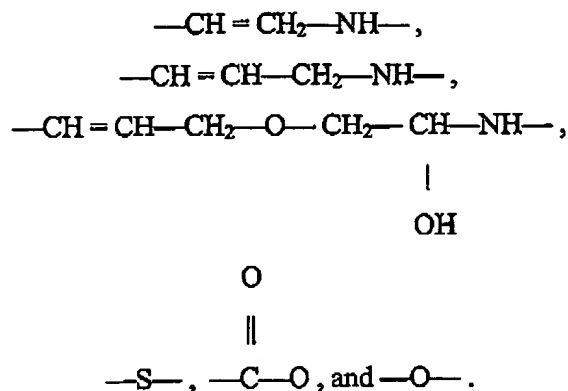
— September 19, 2005]

Claim 1072 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

Claim 1073 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises: a —CH₂NH— moiety, an olefinic bond at the α-position relative to the point of attachment to the nucleotide or nucleotide analog structure (i), or both.

Claim 1074 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

Claim 1075 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises or includes an olefinic bond at the α-position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i), or any of the moieties



Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 57 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1076 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises a glycosidic linkage moiety.

Claim 1077 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein in said nucleotide structure or nucleotide analog structure (i), said A is covalently attached to B, and wherein in said nucleotide structure or nucleotide analog structure (ii) or (iii), said Sig is covalently attached to SM or PM through a linkage group.

Claim 1078 (PREVIOUSLY PRESENTED) The process according to claim 1077, wherein, in said nucleotide structure or nucleotide analog structure (i), said linkage group comprises an amine.

Claim 1079 (PREVIOUSLY PRESENTED) The process according to claim 1078, wherein said amine comprises a primary amine.

Claim 1080 (PREVIOUSLY PRESENTED) The process according to claim 1077, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claims 1081-1089 (CANCELED).

Claim 1090 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said A comprises more than three carbon atoms and Sig comprises at least three carbon atoms.

Claim 1091 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said A or said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1092 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 58 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1093 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said A or said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic moiety.

Claim 1094 (PREVIOUSLY PRESENTED) The process according to claim 1093, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claims 1095-1096 (CANCELED).

Claim 1097 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said A or said Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1098 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said A or said Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or any combination of the foregoing.

Claim 1099 (PREVIOUSLY PRESENTED) The process according to claim 1098, wherein said an electron dense component comprises ferritin.

Claim 1100 (CANCELED).

Claim 1101 (PREVIOUSLY PRESENTED) The process according to claim 1098, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claims 1102-1103 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 59 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1104 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein said A or said Sig comprises a sugar residue and said the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 1105 (PREVIOUSLY PRESENTED) The process according to claim 1104, wherein the binding protein comprises a lectin.

Claim 1106 (PREVIOUSLY PRESENTED) The process according to claim 1105, wherein the lectin comprises concanavalin A.

Claim 1107 (PREVIOUSLY PRESENTED) The process according to claim 1105, wherein said lectin is conjugated to ferritin.

Claims 1108-1111 (CANCELED).

Claim 1112 (PREVIOUSLY PRESENTED) The process according to claim 1098, wherein said metal-containing component is catalytic.

Claim 1113 (PREVIOUSLY PRESENTED) The process according to claim 1056, wherein Sig is a non-radioactively detectable indicator molecule.

Claim 1114 (PREVIOUSLY PRESENTED) The process according to claim 1113, wherein said indicator molecule comprises an aromatic structure.

Claim 1115 (PREVIOUSLY PRESENTED) The process according to claim 1114, wherein said aromatic structure is heterocyclic.

Claim 1116 (PREVIOUSLY PRESENTED) The process according to claim 1115, wherein said heterocyclic aromatic structure is fluorescent.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 60 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1117 (PREVIOUSLY PRESENTED) The process according to claim 1116, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or a combination of any of the foregoing.

Claims 1118-1122 (CANCELED).

Claim 1123 (PREVIOUSLY PRESENTED) The process according to claim 1098, wherein said A or said Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claims 1124-1125 (CANCELED).

Claim 1126 (PREVIOUSLY PRESENTED) The process according to claim 1113, wherein said indicator molecule comprises a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

Claims 1127-1162 (CANCELED).

Claim 1163 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said detectable labeled nucleic acid fragments are detectable by a non-radioactive means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1164 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein in said detecting step, the detectable non-radioactive labeled nucleic acid fragments are separated or resolved electrophoretically.

Claim 1165 (PREVIOUSLY PRESENTED) The process according to claims 1025 or 1056, wherein said detecting step is carried out directly.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 61 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1166 (PREVIOUSLY PRESENTED) The process according to claim 1165, wherein the detectable non-radioactive labeled fragments comprise one or more non-radioactively detectable indicator molecules and said direct detection is carried out using these indicator molecules.

Claim 1167 (PREVIOUSLY PRESENTED) The process according to claim 1166, wherein said non-radioactively detectable indicator molecules comprise fluorescently labeled nucleotides.

Claim 1168 (PREVIOUSLY PRESENTED) The process according to claim 1167, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1169 (PREVIOUSLY PRESENTED) The process according to claim 1165, wherein said detecting step is carried out by means of a directly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Claim 1170 (PREVIOUSLY PRESENTED) The process according to claim 1165, wherein in said detecting step the directly detectable signal comprises a chelating structure, a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Claim 1171 (CANCELED).

Claim 1172 (PREVIOUSLY PRESENTED) The process according to claims 1025 or 1056, wherein said detecting step is carried out by means of an indirectly detectable signal provided by said one or more non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs, said A or said Sig detectable non-radioactive moiety.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 62 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1173 (PREVIOUSLY PRESENTED) The process according to claim 1172, wherein in said detecting step the indirectly detectable signal an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 1174 (CANCELED).

Claim 1175 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said one or more modified or labeled nucleotides or modified or labeled nucleotide analogs are capable of being detected by an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1176 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said detecting step comprises localizing said detectable non-radioactive labeled nucleic acid fragments by means of said one or more modified or labeled nucleotides or modified or labeled nucleotide analogs.

Claim 1177 (PREVIOUSLY PRESENTED) A process for determining with a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid of interest or a portion thereof, said process comprising:

(A) providing

(1) one or more nucleotides or nucleotide analogs that are: (a) non-radioactive and (b) chemically modified or chemically labeled so as to be detectable provided that said nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid; or

(2) one or more oligonucleotides or polynucleotides comprising at least one of said nucleotides or nucleotide analogs (1); or

(3) both (1) and (2); and

(B) providing at least one nucleic acid of interest;

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

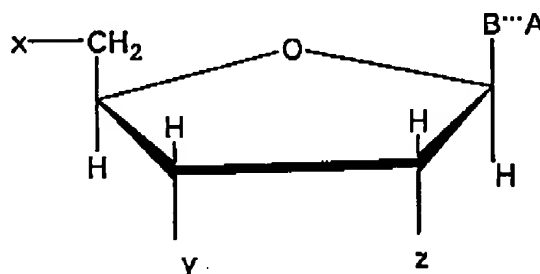
Page 63 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

- September 19, 2005]

wherein said nucleotides or nucleotide analogs (1) and said oligonucleotides and polynucleotides (2) are capable of attaching to, coupling to, or incorporating into, or forming one or more nucleic acid fragments, and wherein said nucleotides or nucleotide analogs (1) have been non-radioactively modified or non-radioactively labeled, non-disruptively or disruptively, on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof; and

(C) incorporating said nucleotides or nucleotide analogs (1) or said oligonucleotides or polynucleotides (2), or both (1) and (2), into or onto one or more of said nucleic acid fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, and wherein said nucleotides or nucleotide analogs (1) comprise a nucleotide structure or nucleotide analog structure comprising one or more of the following :

(i)



wherein B comprises a purine moiety, a 7-deazapurine moiety, or a pyrimidine moiety, and B is covalently bonded to the C1-position of the furanosyl moiety provided that whenever B is a purine moiety or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or of the 7-deazapurine moiety and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety capable of producing directly or indirectly a detectable non-radioactive signal; and

wherein B and A are covalently attached directly or through a linkage group, and

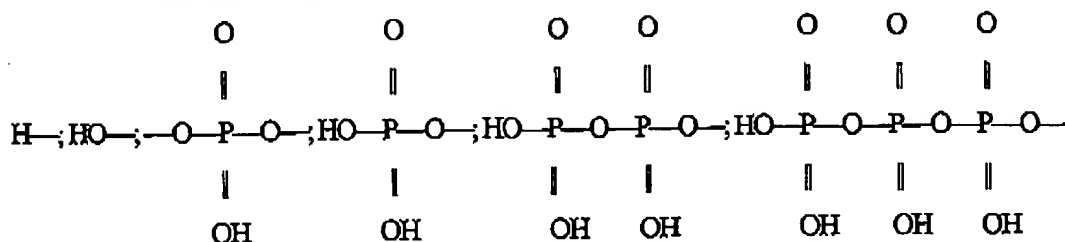
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

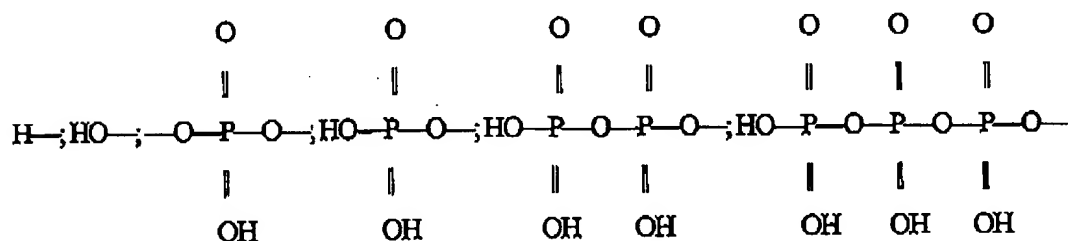
Page 64 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

wherein x comprises:

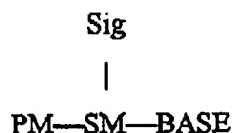


wherein y comprises:



wherein z comprises H-orHO-;

(ii)



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety, or

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 65 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

(D) transferring or subjecting said detectable non-radioactive labeled fragments to a sequencing gel;

(E) separating or resolving said detectable non-radioactive labeled fragments; and

(F) non-radioactively detecting directly or indirectly the presence of said detectable non-radioactive labeled fragments to determine the sequence of said nucleic acid of interest.

Claim 1178 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein the nucleic acid sequence of interest is derived from an organism.

Claim 1179 (PREVIOUSLY PRESENTED) The process according to claim 1178, wherein said organism comprises bacteria, fungi, viruses, yeast, mammals, or a combination of any of the foregoing.

Claim 1180 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 66 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1181 (PREVIOUSLY PRESENTED) The process according to claim 1179, wherein said mammals comprise human beings.

Claim 1182 (PREVIOUSLY PRESENTED) The process according to claim 1178, wherein said organism is living.

Claim 1183 (PREVIOUSLY PRESENTED) The process according to claims 1178 or 1182, wherein said organism comprises prokaryotes or eukaryotes.

Claim 1184 (CANCELED).

Claim 1185 (PREVIOUSLY PRESENTED) The process according to claim 1183, wherein said eukaryotic nucleic acid sequence of interest comprises a mammalian nucleic acid sequence contained within a chromosome.

Claims 1186-1189 (CANCELED).

Claim 1190 (PREVIOUSLY PRESENTED) The process according to claim 1185, wherein said mammalian chromosomal nucleic acid sequence comprises a human chromosomal nucleic acid sequence that is part of a human gene library.

Claim 1191 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said incorporating step is carried out using an enzyme.

Claim 1192 (PREVIOUSLY PRESENTED) The process according to claim 1191, wherein said enzyme comprises a polymerase.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 67 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1193 (PREVIOUSLY PRESENTED) The process according to claim 1192, wherein said polymerase comprises DNA polymerase.

Claim 1194 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said nucleotides or nucleotide analogs (1) comprise a nucleoside di- or tri-phosphate.

Claim 1195 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said incorporating step is template dependent or template independent.

Claim 1196 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said incorporating step is template dependent.

Claim 1197 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one internal modified nucleotide or internal modified nucleotide analog (1).

Claim 1198 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein the detectable labeled nucleic acid fragments prepared by said incorporating step comprises at least one terminal modified nucleotide or terminal modified nucleotide analog (1).

Claim 1199 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said nucleotide analog has been attached terminally to DNA or RNA by means of an enzyme.

Claim 1200 (PREVIOUSLY PRESENTED) The process according to claim 1199, wherein said enzyme comprises terminal transferase.

Claims 1201-1203 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 68 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1204 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said incorporation comprises nick translation.

Claims 1205-1207 (CANCELED).

Claim 1208 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein PM comprises a monophosphate, a di-phosphate, a tri-phosphate or a tetra-phosphate.

Claim 1209 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a nucleoside mono-, di- or tri-phosphate.

Claims 1210-1211 (CANCELED).

Claim 1212 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein SM comprises ribose, 2'-deoxyribose, 3'-deoxyribose or 2', 3'-dideoxyribose.

Claim 1213 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein B in said nucleotide structure or nucleotide analog structure (i), and BASE in nucleotide structure or nucleotide analog structure (ii) or (iii), comprises a pyrimidine moiety, a purine moiety, a 7-deazapurine moiety, or a combination of any of the foregoing.

Claim 1214 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said nucleotide structure or nucleotide analog structure (i): when B is a purine, A is attached to the 8-position of the purine moiety; when B is a 7-deazapurine moiety, A is attached to the 7-position of the deazapurine moiety; and when B is a pyrimidine moiety, A is attached to the 5-position of the pyrimidine moiety.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 69 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1215 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said nucleotide or nucleotide analog structure (i), A is covalently attached to B at the C5 position, the C2 position, the N3 position, the C6 position, or combinations thereof when B is a pyrimidine, or is covalently attached to B at the C8 position, the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, or combinations thereof, when B is a purine, or is covalently attached to the 7-position when b is a 7-deazapurine.

Claim 1216 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said nucleotide structure or nucleotide analog structure (i) A is covalently attached to B at a position comprising the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, or combinations thereof.

Claim 1217 (CANCELED).

Claim 1218 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said incorporating step, A in the nucleotide structure or nucleotide analog structure (i) is covalently attached to B through a linkage group.

Claim 1219 (PREVIOUSLY PRESENTED) The process according to claim 1218, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1220 (PREVIOUSLY PRESENTED) The process according to claim 1218, wherein, in nucleotide structure or nucleotide analog structure (i), said linkage group comprises an amine.

Claim 1221 (PREVIOUSLY PRESENTED) The process according to claim 1220, wherein said amine comprises a primary amine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 70 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1222 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said incorporating step, Sig in the nucleotide structure or nucleotide analog structure (ii) is covalently attached to SM through a linkage group.

Claim 1223 (PREVIOUSLY PRESENTED) The process according to claim 1222, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1224 (PREVIOUSLY PRESENTED) The process according to claim 1222, wherein, in nucleotide structure or nucleotide analog structure (i), said linkage group comprises an amine.

Claim 1225 (PREVIOUSLY PRESENTED) The process according to claim 1224, wherein said amine comprises a primary amine.

Claim 1226 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said incorporating step, Sig in the nucleotide structure or nucleotide analog structure (iii) is covalently attached to PM through a linkage group.

Claim 1227 (PREVIOUSLY PRESENTED) The process according to claim 1226, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1228 (PREVIOUSLY PRESENTED) The process according to claim 1226, wherein, in nucleotide structure or nucleotide analog structure (i), said linkage group comprises an amine.

Claim 1229 (PREVIOUSLY PRESENTED) The process according to claim 1228, wherein said amine comprises a primary amine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

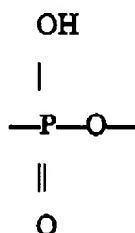
Page 71 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)]

— September 19, 2005]

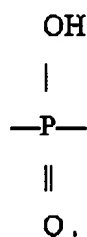
Claim 1230 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said nucleotide structure or nucleotide analog structure (ii), PM is attached to SM at the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1231 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said nucleotide structure or nucleotide analog structure (iii), PM is attached to SM at the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1232 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said covalent attachment in nucleotide structure or nucleotide analog structure (iii) comprises:



or



Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 72 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1233 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein PM comprises a mono-, di- or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), the Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 1234 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said covalent attachment in any of nucleotide structure or nucleotide analog structure (i), (ii) or (iii) does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

1235 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises a —CH₂NH— moiety, an olefinic bond at the α -position relative to the point of attachment to the nucleotide structure or nucleotide analog structure (i), or both.

Claim 1236 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises an allylamine group.

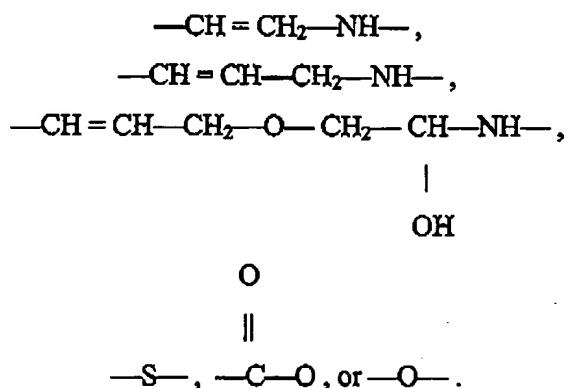
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 73 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1237 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein, in said nucleotide structure or nucleotide analog structure (i), said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



Claim 1238 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein, in said nucleotide or nucleotide analog structure (i), said covalent attachment comprises a glycosidic linkage moiety.

Claim 1239 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein in said nucleotide structure or nucleotide analog structure (i), A is covalently attached to B through a linkage group, or in said nucleotide structure or nucleotide analog structure (ii) or (iii), Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1240 (PREVIOUSLY PRESENTED) The process according to claim 1239, wherein, in said nucleotide structure or nucleotide analog structure (i), said linkage group comprises an amine.

Claim 1241 (PREVIOUSLY PRESENTED) The process according to claim 1240, wherein said amine comprises a primary amine.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 74 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1242 (PREVIOUSLY PRESENTED) The process according to claim 1239, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1243 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said Sig comprises at least three carbon atoms.

Claim 1244 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said A or Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claims 1245-1247 (CANCELED).

Claim 1248 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said A or Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Claim 1249 (PREVIOUSLY PRESENTED) The process according to claim 1177, where said A or Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component a chelating component or any combination thereof.

Claims 1250-1252 (CANCELED).

Claim 1253 (PREVIOUSLY PRESENTED) The process according to claim 1249, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 1254 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 75 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1255 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said A or Sig comprises a sugar residue and the sugar residue is capable of complexing with a sugar binding protein or a polysaccharide binding protein.

Claim 1256 (PREVIOUSLY PRESENTED) The process according to claim 1255, wherein the binding protein comprises a lectin.

Claim 1257 (PREVIOUSLY PRESENTED) The process according to claim 1256, wherein the lectin comprises concanavalin A.

Claim 1258 (PREVIOUSLY PRESENTED) The process according to claim 1256, wherein said lectin is conjugated to ferritin.

Claims 1259-1262 (CANCELED).

Claim 1263 (PREVIOUSLY PRESENTED) The process according to claim 1249, wherein said metal-containing component is catalytic.

Claim 1264 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein A or Sig is a non-radioactively detectable indicator molecule.

Claim 1265 (PREVIOUSLY PRESENTED) The process according to claim 1264, wherein said indicator molecule comprises an aromatic structure.

Claim 1266 (PREVIOUSLY PRESENTED) The process according to claim 1265, wherein said aromatic structure is heterocyclic.

Claim 1267 (PREVIOUSLY PRESENTED) The process according to claim 1266, wherein said heterocyclic aromatic structure is fluorescent.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 76 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1268 (PREVIOUSLY PRESENTED) The process according to claim 1267, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or any combination thereof.

Claim 1269 (PREVIOUSLY PRESENTED) The process according to claim 1268, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1270 (PREVIOUSLY PRESENTED) The process according to claim 1264, wherein said indicator molecule comprises a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

Claim 1271 (CANCELED).

Claim 1272 (PREVIOUSLY PRESENTED) The process according to claim 1249, wherein said fluorescent component fluorescein, rhodamine, dansyl or any combination thereof.

Claims 1273-1274 (CANCELED).

Claim 1275 (PREVIOUSLY PRESENTED) The process according to claim 1249, wherein said A or Sig comprises an antigenic or hapten component capable of complexing with an antibody specific to the component.

Claims 1276-1277 (CANCELED).

Claim 1278 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein any of said nucleotide structure or nucleotide analog structure (i), (ii) and (iii) is detectable by a means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 77 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1279 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said A or Sig is detectable when it is attached to the nucleotide structure or nucleotide analog structure (i), (ii) or (iii) directly or through a linkage group.

Claim 1280 (PREVIOUSLY PRESENTED) The process according to claim 1279, wherein said linkage group does not interfere substantially with the characteristic ability of A or Sig to form a detectable non-radioactive signal.

Claim 1281 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said detectable non-radioactive labeled nucleic acid fragment or fragments are terminally ligated or attached to a polypeptide.

Claim 1282 (PREVIOUSLY PRESENTED) The process according to claim 1281, wherein said polypeptide comprises a polylysine.

Claim 1283 (PREVIOUSLY PRESENTED) The process according to claim 1281, wherein said polypeptide comprises avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1284 (PREVIOUSLY PRESENTED) The process according to claim 1281, wherein said A or Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1285 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said separating step is carried out electrophoretically.

Claim 1286 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said detecting step is carried out directly.

Claim 1287 (PREVIOUSLY PRESENTED) The process according to claim 1286, wherein said direct detection is carried out on one or more non-radioactively detectable indicator molecules.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 78 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1288 (PREVIOUSLY PRESENTED) The process according to claim 1287, wherein said non-radioactively detectable indicator molecules comprise fluorescently labeled nucleotides.

Claim 1289 (PREVIOUSLY PRESENTED) The process according to claim 1288, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1290 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said detecting step is carried out by means of a directly detectable signal provided by said A or Sig detectable non-radioactive moiety.

Claim 1291 (PREVIOUSLY PRESENTED) The process according to claim 1290, wherein in said detecting step, the directly detectable signal providing A or Sig detectable non-radioactive moiety comprises a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Claim 1292 (PREVIOUSLY PRESENTED) The process according to claim 1290, wherein in said detecting step the directly detectable signal is provided by an enzyme.

Claim 1293 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said A or Sig detectable non-radioactive moiety.

Claim 1294 (PREVIOUSLY PRESENTED) The process according to claim 1293, wherein in said detecting step, the indirectly detectable signal is provided by a member which comprises an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 1295 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 79 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1296 (PREVIOUSLY PRESENTED) The process according to claim 1293, wherein in said detecting step, the indirectly detectable signal providing Sig comprises a structure capable of binding to an insoluble phase.

Claim 1297 (PREVIOUSLY PRESENTED) The process according to claim 1177, wherein said Sig detectable non-radioactive moiety is capable of being detected by means comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claims 1298-1410 (CANCELED).

Claim 1411 (PREVIOUSLY PRESENTED) A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (A) providing a sample which may contain a nucleic acid of interest;
- (B) providing:
 - (i) an oligo- or polynucleotide that comprises two segments, the first segment comprising a nucleotide sequence that is complementary to and capable of specifically hybridizing to and forming a hybrid with said nucleic acid of interest or a portion thereof, and the second segment comprising an operator sequence that is capable of binding to or complexing with a non-radioactively detectable protein; and
 - (ii) a non-radioactively detectable protein which is non-radioactive and has a binding affinity to said operator sequence;
- (C) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide (i) and said non-radioactively detectable protein (ii) to form a complex; and
- (D) detecting non-radioactively the presence of said non-radioactively detectable protein in said complex to detect said nucleic acid of interest.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 80 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1412 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the nucleic acid of interest comprises DNA, RNA or a DNA-RNA hybrid.

Claim 1413 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the nucleic acid of interest is double-stranded or single-stranded.

Claim 1414 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the nucleic acid of interest has been rendered single-stranded.

Claim 1415 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the nucleic acid of interest is derived from an organism.

Claim 1416 (PREVIOUSLY PRESENTED) The process according to claim 1415, wherein the organism comprises prokaryotes or eukaryotes.

Claim 1417 (PREVIOUSLY PRESENTED) The process according to claim 1415, wherein said organism bacteria, fungi, viruses, yeast or mammals.

Claim 1418 (PREVIOUSLY PRESENTED) The process according to claim 1415, wherein said organism is living.

Claim 1419 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the sample is suspected of containing an etiological agent and the nucleic acid of interest is naturally associated with the etiological agent.

Claim 1420 (PREVIOUSLY PRESENTED) The process according to claim 1419, wherein the sample is of human or animal origin and the etiological agent comprises bacteria, virus or fungi.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 81 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1421 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said nucleic acid of interest is derived from an organism comprising *Streptococcus pyrogenes*, *Neisseria meningitides*, *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, or *Mycobacterium tuberculosis*.

Claim 1422 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said one or more oligo- or polynucleotides are derived from *Neisseria gonorrhoeae* sequences.

Claim 1423 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the sample comprises a bacterium suspected of containing a nucleic acid of interest which imparts resistance to an antibiotic and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the sequence of the bacterium which confers resistance to the antibiotic.

Claim 1424 (PREVIOUSLY PRESENTED) The process according to claim 1423, wherein when said bacterium is *Streptococcus pyrogenes* or *Neisseria meningitidis*, said antibiotic is penicillin, wherein when said bacterium is *Staphylococcus aureus*, *Candida albicans*, *Pseudomonas aeruginosa*, *Streptococcus pyrogenes*, or *Neisseria gonorrhoea*, said antibiotic is a tetracycline, and wherein when said bacterium is *Mycobacterium tuberculosis*, said antibiotic is an aminoglycoside.

Claim 1425 (PREVIOUSLY PRESENTED) The process according to claim 1424, wherein said bacterium is *Neisseria gonorrhoeae* and said antibiotic comprises penicillin, tetracycline, aminoglycoside or combinations thereof.

Claim 1426 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein the sample is suspected of containing a nucleic acid of interest associated with a genetic disorder and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid associated with the genetic disorder.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 82 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1427 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said sample is suspected of containing a nucleic acid of interest associated with thalassemia and wherein the oligo- or polynucleotide comprises a polynucleotide complementary to the nucleic acid which is absent in the thalassemic subjects.

Claim 1428 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said process is utilized for chromosomal karyotyping which comprises contacting the sample with a series of the oligo- or polynucleotides (i) which are complementary to a series of known genetic sequences located on chromosomes.

Claim 1429 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said process is utilized to determine the number of copies of an individual chromosome in a sample.

Claim 1430 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said non-radioactive detectable protein comprises an antibody, a promoter, a repressor or an inducer.

Claim 1431 (PREVIOUSLY PRESENTED) The process according to claim 1430, wherein said repressor comprises a lac repressor.

Claim 1432 (PREVIOUSLY PRESENTED) The process according to claim 1430, wherein said operator sequence is covalently attached to said oligo- or polynucleotide.

Claim 1433 (PREVIOUSLY PRESENTED) The process according to claim 1432, wherein said covalent attachment has been carried out by ligation.

Claim 1434 (PREVIOUSLY PRESENTED) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to bind to any hybrid formed between said oligo- or polynucleotide and said nucleic acid of interest.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 83 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

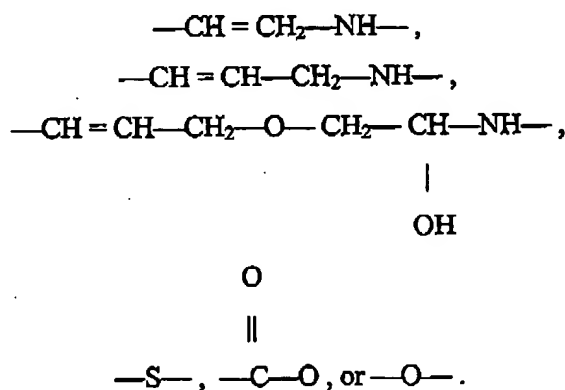
— September 19, 2005]

Claim 1435 (PREVIOUSLY PRESENTED) The process according to claim 1432, wherein said covalent attachment does not interfere substantially with the characteristic ability of said non-radioactively detectable protein to be detected non-radioactively when bound to any hybrid formed between said oligo- or polynucleotide and said nucleic acid of interest.

Claim 1436 (PREVIOUSLY PRESENTED) The process according to claim 1432, wherein said operator sequence is attached via a covalent attachment by an olefinic bond at the α -position relative to the point of attachment to said nucleotide structure or nucleotide analog structure (i), a CH_2NH — moiety, or both.

Claim 1437 (PREVIOUSLY PRESENTED) The process according to claim 1436, wherein said covalent attachment comprises an allylamine group.

Claim 1438 (PREVIOUSLY PRESENTED) The process according to claim 1436, wherein said covalent attachment comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties



Claim 1439 (PREVIOUSLY PRESENTED) The process according to claim 1432, wherein said covalent attachment comprises a glycosidic linkage moiety.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 84 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1440 (PREVIOUSLY PRESENTED) The process according to claim 1432, wherein said operator sequence is covalently attached to any of the base, phosphate, or furanosyl moieties in said oligo- or polynucleotide.

Claim 1441 (PREVIOUSLY PRESENTED) The process according to claim 1440, wherein said covalent attachment is through a linkage group.

Claim 1442 (PREVIOUSLY PRESENTED) The process according to claim 1441, wherein said linkage group comprises an amine.

Claim 1443 (PREVIOUSLY PRESENTED) The process according to claim 1442, wherein said amine comprises a primary amine.

Claim 1444 (PREVIOUSLY PRESENTED) The process according to claim 1441, wherein said linkage group does not substantially interfere with the binding of said non-radioactively detectable protein to said operator sequence.

Claim 1445 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said non-radioactively detectable protein comprises a signalling component or indicator molecule.

Claim 1446 (PREVIOUSLY PRESENTED) The process according to claim 1445, wherein said signalling component or indicator molecule comprises at least three carbon atoms.

Claim 1447 (PREVIOUSLY PRESENTED) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 85 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1448 (PREVIOUSLY PRESENTED) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aliphatic chemical moiety comprising at least four carbon atoms.

Claim 1449 (PREVIOUSLY PRESENTED) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1450 (PREVIOUSLY PRESENTED) The process according to claim 1449, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1451 (PREVIOUSLY PRESENTED) The process according to claim 1446, wherein said signalling component or indicator molecule comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1452 (PREVIOUSLY PRESENTED) The process according to claim 1451, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1453 (PREVIOUSLY PRESENTED) The process according to claim 1446, wherein said signalling component or indicator molecule comprises a monosaccharide, polysaccharide or an oligosaccharide.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 86 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1454 (PREVIOUSLY PRESENTED) The process according to claim 1445, wherein said signalling component or indicator molecule comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component a chelating component, or any combination of any of the foregoing.

Claim 1455 (PREVIOUSLY PRESENTED) The process according to claim 1445, wherein said signalling component or indicator molecule comprises an aromatic structure.

Claim 1456 (PREVIOUSLY PRESENTED) The process according to claim 1455, wherein said aromatic structure is heterocyclic.

Claim 1457 (PREVIOUSLY PRESENTED) The process according to claim 1456, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1458 (PREVIOUSLY PRESENTED) The process according to claim 1457, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl or any combination of any of the foregoing.

Claim 1459 (PREVIOUSLY PRESENTED) The process according to claim 1458, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1460 (PREVIOUSLY PRESENTED) The process according to claim 1454, wherein said signalling component or indicator molecule comprises a chemiluminescent component.

Claim 1461 (PREVIOUSLY PRESENTED) The process according to claim 1454, wherein said signalling component or indicator molecule comprises a chelating component.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 87 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1462 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable by a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1463 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said non-radioactively detectable protein is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex formed with said nucleic acid of interest.

Claim 1464 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said nonradioactively detectable protein is detectable when it is attached to said oligo- or polynucleotide directly or through a linkage group.

Claim 1465 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said oligo- or polynucleotide is contacted with said sample suspected of containing the nucleic acid of interest prior to forming a complex with said non-radioactively detectable protein.

Claim 1466 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said detecting step is carried out directly.

Claim 1467 (PREVIOUSLY PRESENTED) The process according to claim 1466, wherein said direct detection of the non-radioactively detectable protein is carried out on one or more signalling components or indicator molecules.

Claim 1468 (PREVIOUSLY PRESENTED) The process according to claim 1467, wherein said direct detection step is carried out by a fluorogenic structure, a chemiluminescent structure, an enzyme, or an electron dense structure.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 88 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1469 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said detecting step is carried out indirectly.

Claim 1470 (PREVIOUSLY PRESENTED) The process according to claim 1469, wherein said indirect detection is carried out by a means comprising an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, a structure capable of binding to an insoluble phase, or a combination of any of the foregoing.

Claim 1471 (PREVIOUSLY PRESENTED) The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by means comprising an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1472 (PREVIOUSLY PRESENTED) The process according to claim 1411, further comprising one or more washing steps.

Claim 1473 (PREVIOUSLY PRESENTED) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising:

providing at least one cell;

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise:

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 89 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

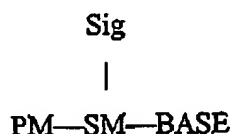
SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety; and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

Enz-5(D8)(C2)

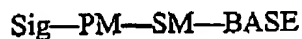
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 90 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting non-radioactively any specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome, and determining whether the number of copies of said particular chromosome in said cell is abnormal.

Claim 1474 (PREVIOUSLY PRESENTED) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising:

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

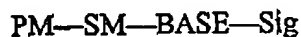
Page 91 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

providing at least one cell;

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

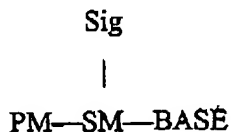
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 92 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

wherein

PM is a phosphate moiety,

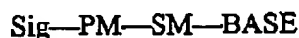
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides,

permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 93 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

detecting non-radioactively any of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

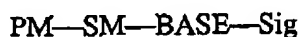
identifying said chromosome of interest by means of said hybridization pattern obtained.

Claim 1475 (PREVIOUSLY PRESENTED) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising:

providing at least one cell;

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein said clones or fragments or said oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets are labeled with a different indicator moiety and each of said clones or DNA fragments or oligo- or polynucleotides comprises one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise:

(i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

Enz-5(D8)(C2)

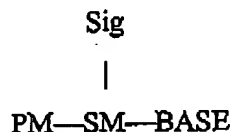
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 94 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
— September 19, 2005]

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

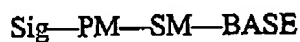
SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 95 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

BASE is a base moiety and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group ;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting non-radioactively any of said different indicator moieties in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying any one of the chromosomes in said cell of interest.

Claim 1476 (PREVIOUSLY PRESENTED) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising:

providing at least one interphase cell;

providing sets of clones or DNA fragments or oligo- or polynucleotides derived from said clones, wherein said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest and each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more of :

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 96 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

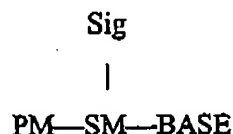
SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 97 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a detectable non-radioactive moiety,

wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides,

permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes;

detecting non-radioactively any of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and

comparing each generated signal with other generated signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

Claim 1477 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog has been attached terminally to DNA or RNA by means of an enzyme.

Claim 1478 (PREVIOUSLY PRESENTED) The process according to claim 1477, wherein said enzyme comprises terminal transferase.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 98 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1479 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said nucleotide analog has been coupled to DNA or RNA by a coupling means comprising chemical coupling or enzymatic coupling.

Claim 1480 (PREVIOUSLY PRESENTED) The process according to claim 1479, wherein said chemical coupling has been carried out by a chemical coupling means comprising carbodiimide or formaldehyde.

Claim 1481 (PREVIOUSLY PRESENTED) The process according to claim 1479, wherein said enzymatic coupling has been carried out by an enzymatic coupling means comprising DNA ligase or RNA ligase.

Claim 1482 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation comprises nick translation.

Claim 1483 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said incorporation is carried out by means of a polymerizing enzyme.

Claim 1484 (PREVIOUSLY PRESENTED) The process according to claim 1483, wherein said polymerizing enzyme comprises a polymerase.

Claim 1485 (PREVIOUSLY PRESENTED) The process according to claim 1484, wherein said polymerase comprises DNA polymerase or RNA polymerase.

Claim 1486 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM comprises a mono-phosphate, a di-phosphate, a tri-phosphate or a tetraphosphate.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 99 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1487 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises nucleoside mono-, di- or tri-phosphate.

Claims 1488-1489 (CANCELED).

Claim 1490 (PREVIOUSLY PRESENTED) The process according to claim 1473, 1474, 1475 or 1476, wherein SM comprises ribose, 2'-deoxyribose, 3'-deoxyribose or 2', 3'-dideoxyribose.

Claim 1491 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein BASE in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) comprises a 7-deazapurine.

Claim 1492 (CANCELED).

Claim 1493 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (i) is covalently attached to BASE the C2 position, the N3 position, the C6 position, or combinations thereof when BASE is a pyrimidine, or is covalently attached to BASE the N1 position, the C2 position, the N3 position, the C6 position, the N7 position, or combinations thereof when BASE is a purine.

Claim 1494 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (i) is covalently attached to BASE at a position comprising the N⁴ position when said pyrimidine comprises cytosine, the N² position when said purine comprises adenine or deazaadenine, the N⁶ position when said purine comprises guanine or deazaguanine, or combinations thereof.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

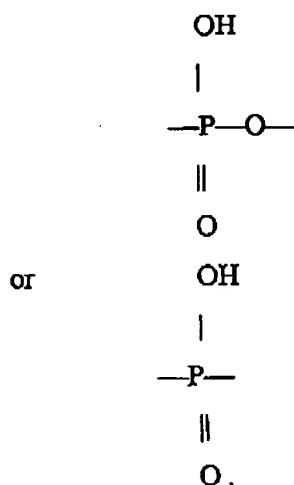
Page 100 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1495 (PREVIOUSLY PRESENTED) The process according to claim 1473, 1474, 1475 or 1476, wherein in said nucleotide structure or nucleotide analog structure (ii), PM is attached to SM at the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1496 (PREVIOUSLY PRESENTED) The process according to claim 1473, 1474, 1475 or 1476, wherein in said nucleotide structure or nucleotide analog structure (iii), PM is attached to SM at the 2', 3', 5' positions, or any combination thereof, and BASE is attached to the 1' position of SM from the N1 position when BASE is a pyrimidine or the N9 position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization.

Claim 1497 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in nucleotide or nucleotide analog structure (iii) comprises



Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 101 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1498 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein PM comprises a mono-, di or tri-phosphate, and wherein in said nucleotide structure or nucleotide analog structure (iii), Sig is covalently attached to PM through a phosphorus or phosphate oxygen.

Claim 1499 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said covalent attachment in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) does not interfere substantially with the characteristic ability of Sig to form a detectable non-radioactive signal.

Claims 1500-1503 (CANCELED).

Claim 1504 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein in any of said nucleotide structures or nucleotide analog structures (i), (ii) or (iii) said Sig is covalently attached to BASE, SM or PM through a linkage group.

Claim 1505 (PREVIOUSLY PRESENTED) The process according to claim 1504, wherein, in nucleotide structure or nucleotide analog structure (i), said linkage group contains an amine.

Claim 1506 (PREVIOUSLY PRESENTED) The process according to claim 1505, wherein said amine comprises a primary amine.

Claim 1507 (PREVIOUSLY PRESENTED) The process according to claim 1504, wherein said linkage group does not substantially interfere with formation of the signalling moiety or detection of the detectable non-radioactive signal.

Claim 1508 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises at least three carbon atoms.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 102 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1509 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least three carbon atoms and at least one double bond.

Claim 1510 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aliphatic chemical moiety comprising at least four carbon atoms.

Claim 1511 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least five carbon atoms.

Claim 1512 (PREVIOUSLY PRESENTED) The process according to claim 1511, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1513 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety comprises an aromatic or cycloaliphatic group comprising at least six carbon atoms.

Claim 1514 (PREVIOUSLY PRESENTED) The process according to claim 1513, wherein said aromatic or cycloaliphatic moiety is fluorescent or chemiluminescent.

Claim 1515 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a monosaccharide, polysaccharide or an oligosaccharide.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 103 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1516 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component, or any combination of any of the foregoing.

Claim 1517 (CANCELED).

Claim 1518 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein said electron dense component comprises ferritin.

Claim 1519 (CANCELED).

Claim 1520 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein said magnetic component comprises magnetic oxide or magnetic iron oxide.

Claim 1521 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein said magnetic component comprises magnetic beads.

Claim 1522 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig comprises a sugar residue and the sugar residue is complexed with or attached to a sugar binding protein or a polysaccharide binding protein.

Claim 1523 (PREVIOUSLY PRESENTED) The process according to claim 1522, wherein the binding protein comprises a lectin.

Claim 1524 (PREVIOUSLY PRESENTED) The process according to claim 1523, wherein the lectin comprises concanavalin A.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 104 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1525 (PREVIOUSLY PRESENTED) The process according to claim 1523, wherein said lectin is conjugated to ferritin.

Claim 1526 (CANCELED).

Claim 1527 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein said enzyme comprises alkaline phosphatase, acid phosphatase, galactosidase, ribonuclease, glucose oxidase and peroxidase, or a combination thereof.

Claims 1528-1529 (CANCELED).

Claim 1530 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein said metal-containing component is catalytic.

Claim 1531 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is a non-radioactively detectable indicator molecule.

Claim 1532 (PREVIOUSLY PRESENTED) The process according to claim 1531, wherein said indicator molecule comprises an aromatic structure.

Claim 1533 (PREVIOUSLY PRESENTED) The process according to claim 1532, wherein said aromatic structure is heterocyclic.

Claim 1534 (PREVIOUSLY PRESENTED) The process according to claim 1533, wherein said heterocyclic aromatic structure is fluorescent.

Claim 1535 (PREVIOUSLY PRESENTED) The process according to claim 1534, wherein the fluorescent heterocyclic aromatic structure comprises fluorescein, rhodamine, dansyl, or a combination of any of the foregoing.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 105 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
— September 19, 2005]

Claim 1536 (PREVIOUSLY PRESENTED) The process according to claim 1535, wherein said fluorescent heterocyclic aromatic structure comprises fluorescein.

Claim 1537 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein Sig comprises a fluorescent component.

Claim 1538 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein said fluorescent component comprises fluorescein, rhodamine or dansyl.

Claim 1539 (PREVIOUSLY PRESENTED) The process according to claim 1538, wherein said fluorescent component comprises fluorescein.

Claim 1540 (CANCELED).

Claim 1541 (PREVIOUSLY PRESENTED) The process according to claim 1516, wherein Sig comprises an antigenic or hapten component capable of completing with an antibody specific to the component.

Claims 1542-1543 (CANCELED).

Claim 1544 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is a non-radioactively detectable indicator molecule.

Claim 1545 (PREVIOUSLY PRESENTED) The process according to claim 1544, wherein said indicator molecule comprises a fluorescent component, a chemiluminescent component, a chelating component, or a combination of any of the foregoing.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 106 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

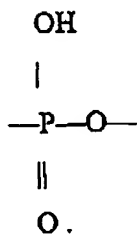
Claim 1546 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein any of said nucleotide structures or nucleotide analog structures (i), (ii) and (iii) are detectable by a means comprising a fluorescent measurement, a chemiluminescent measurement, or a combination thereof.

Claim 1547 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when the oligo- or polynucleotide is contained in a double-stranded ribonucleic or deoxyribonucleic acid duplex.

Claim 1548 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig is detectable when it is attached to the nucleotide directly or through a linkage group.

Claim 1549 (PREVIOUSLY PRESENTED) The process according to claim 1548, wherein said linkage group does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

Claim 1550 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (iii) is covalently attached to PM via the chemical linkage



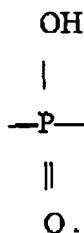
Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 107 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1551 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein Sig in said nucleotide structure or nucleotide analog structure (iii) is covalently attached to PM via a chemical linkage.



Claim 1552 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein the oligo- or polynucleotide is terminally ligated or attached to a polypeptide.

Claim 1553 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising contacting the sample with a polypeptide capable of forming a complex with Sig and a moiety which can be detected when the complex is formed.

Claim 1554 (PREVIOUSLY PRESENTED) The process according to claim 1552, wherein the polypeptide comprises a polylysine.

Claim 1555 (PREVIOUSLY PRESENTED) The process according to claim 1553, wherein the polypeptide comprises a polylysine.

Claim 1556 (PREVIOUSLY PRESENTED) The process according to claim 1552, wherein the polypeptide comprises avidin, streptavidin or anti-Sig immunoglobulin.

Claim 1557 (PREVIOUSLY PRESENTED) The process according to claim 1553, wherein the polypeptide comprises avidin, streptavidin or anti-Sig immunoglobulin.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 108 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1558 (PREVIOUSLY PRESENTED) The process according to claim 1553, wherein Sig comprises a ligand and the polypeptide comprises an antibody thereto.

Claim 1559 (PREVIOUSLY PRESENTED) The process according to claim 1553, wherein the moiety which can be detected when the complex is formed comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component, or any combination of any of the foregoing.

Claim 1560 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out directly.

Claim 1561 (PREVIOUSLY PRESENTED) The process according to claim 1560, wherein said direct detection is carried out on one or more non-radioactively detectable indicator molecules.

Claim 1562 (PREVIOUSLY PRESENTED) The process according to claim 1561, wherein said non-radioactively detectable indicator molecules comprise fluorescently labeled nucleotides.

Claim 1563 (PREVIOUSLY PRESENTED) The process according to claim 1562, wherein said fluorescently labeled nucleotides comprise fluorescent DNA.

Claim 1564 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a directly detectable signal provided by said Sig detectable non-radioactive moiety.

Claim 1565 (PREVIOUSLY PRESENTED) The process according to claim 1564, wherein said detecting step is carried out by a fluorogenic structure, a chemiluminescent structure or an electron dense structure.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 109 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1566 (PREVIOUSLY PRESENTED) The process according to claim 1564, wherein said detecting step the directly detectable non-radioactive signal is provided by an enzyme.

Claim 1567 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said detecting step is carried out by means of a indirectly detectable signal provided by said Sig detectable non-radioactive moiety.

Claim 1568 (PREVIOUSLY PRESENTED) The process according to claim 1567, wherein said detecting step the indirectly detectable non-radioactive signal is provided by an antibody, an antigen, a hapten, a receptor, a ligand or an enzyme.

Claim 1569 (CANCELED).

Claim 1570 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1571 (PREVIOUSLY PRESENTED) The process according to any of claims 1473, 1474, 1475 or 1476, further comprising one or more washing steps.

Claim 1572 (PREVIOUSLY PRESENTED) The process according to claim 1473, 1474, 1475 or 1476, wherein said one or more clones or DNA fragments or oligo- or polynucleotides derived from clone or clones are derived from said particular chromosome or said chromosome of interest or said chromosome in said interphase cell of interest.

Claim 1573 (PREVIOUSLY PRESENTED) The process according to claim 1475, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 110 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1574 (PREVIOUSLY PRESENTED) The process according to any of claims. 1473, 1474 or 1475, wherein said detecting step is carried out by a means comprising manual means or automatic means.

Claim 1575 (PREVIOUSLY PRESENTED) The process according to claim 1574, wherein said manual means comprises visualization.

Claim 1576 (PREVIOUSLY PRESENTED) The process according to claim 1574, wherein said automatic means comprises computerized automatic karyotyping.

Claim 1577 (PREVIOUSLY PRESENTED) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with the same indicator molecule.

Claim 1578 (PREVIOUSLY PRESENTED) The process according to claim 1476, wherein each of said sets of clones or DNA fragments or oligo- or polynucleotides is labeled with a different indicator molecule.

Claim 1579 (PREVIOUSLY PRESENTED) The process according to claim 1476, wherein said detecting and determining step is carried out by a means comprising manual means or automatic means.

Claim 1580 (PREVIOUSLY PRESENTED) The process according to claim 1579, wherein said manual means comprises visualization.

Claim 1581 (PREVIOUSLY PRESENTED) The process according to claim 1579, wherein said automatic means comprises computerized automatic karyotyping.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 111 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claims 1582-1699 (CANCELED)

Claim 1700 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a sample comprising a nucleic acid of interest;

providing a metal or metal ion;

providing or generating non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs has been attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating said metal or metal ion and providing a detectable signal, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;

and

detecting the presence of each of said separated or resolved fragments by detecting the signal provided by said metal or metal ion chelated by said chelating structure or chelating components; and

determining the sequence of said nucleic acid of interest.

Claim 1701. (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a sample comprising a nucleic acid of interest;

providing a metal or metal ion;

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 112 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating said metal or metal ion and providing a detectable signal, and wherein said detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof;

introducing or subjecting said fragments to a sequencing gel;

separating or resolving said fragments in said sequencing gel; and

detecting each of the separated or resolved fragments by detecting the signal provided by said metal or metal ion chelated by said chelating structure or chelating components in the modified or labeled nucleotides or modified or labeled nucleotide analogs; and

determining the sequence of said nucleic acid of interest.

Claim 1702. (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing a sample comprising a nucleic acid of interest;

providing a metal or metal ion;

providing or generating detectable non-radioactive labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs has been attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating said metal or metal ion and providing a detectable signal, and wherein said detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof;

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 113 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

detecting with a sequencing gel the detectable non-radioactive labeled nucleic acid fragments by means of said metal or metal ion chelated by said chelating structure or chelating components; and

determining the sequence of said nucleic acid of interest.

Claim 1703. (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising detecting with a sequencing gel one or more detectable non-radioactive labeled nucleic acid fragments comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise one or more chelating structures or chelating components capable of chelating said metal or metal ion and providing a detectable signal, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof.

Claim 1704. (PREVIOUSLY PRESENTED) A process for determining in a sequencing gel the presence of nucleic acid fragments comprising a sequence complementary to a nucleic acid sequence of interest or a portion thereof, said process comprising:

- (A) providing a sample which may comprise a nucleic acid of interest;
- (B) providing a metal or metal ion;
- (C) providing
 - (1) one or more detectable non-radioactive chemically modified or chemically labeled nucleotides or detectable non-radioactive chemically modified or chemically labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into a nucleic acid, or

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 114 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

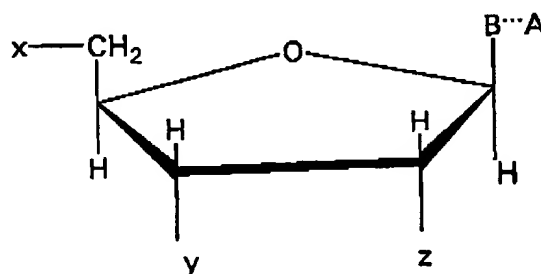
(2) one or more oligonucleotides or polynucleotides comprising at least one of said nucleotides or nucleotide analogs (1); or

(3) both (1) and (2);

wherein said nucleotides or nucleotide analogs (1) and said oligonucleotides and polynucleotides (2) are capable of attaching to or coupling to or incorporating into or forming one or more nucleic acid fragments, wherein said nucleotides or nucleotide analogs (1) comprise one or more chelating structures or chelating components capable of chelating said metal or metal ion and providing a detectable signal, and wherein said nucleotides or nucleotide analogs (1) have been non-radioactively modified or non-radioactively labeled, non-disruptively or disruptively, on the furanosyl moiety, the phosphate moiety, the base moiety, or any combination thereof; and

(D) incorporating said nucleotides or nucleotide analogs (1) or said oligonucleotides or polynucleotides (2), or both (1) and (2), into said nucleic acid fragments, each such fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, and wherein said nucleotides or nucleotide analogs (1) comprise a detectable non-radioactive chemically modified or labeled nucleotide structure, or detectable non-radioactive chemically modified or labeled nucleotide analog structure, selected from the group consisting of one or more of:

(i)



wherein B comprises a purine moiety, a 7-deazapurine moiety, or a pyrimidine moiety, and B is covalently bonded to the C1'-position of the furanosyl moiety provided that whenever B is a purine or a 7-deazapurine moiety, the furanosyl moiety is attached at the N9 position of the purine moiety or the 7-deazapurine moiety, and whenever B is a pyrimidine moiety, the furanosyl moiety is attached at the N1 position of the pyrimidine moiety;

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

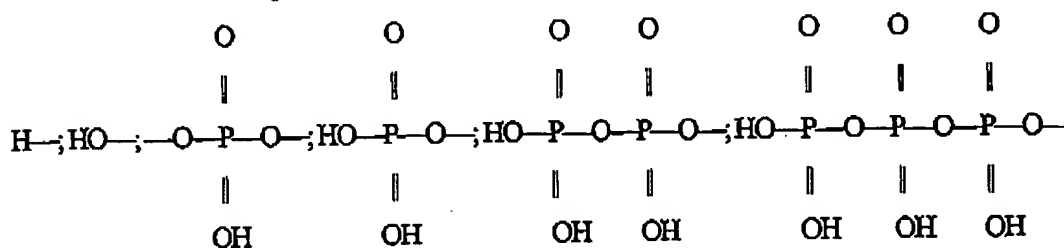
Page 115 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

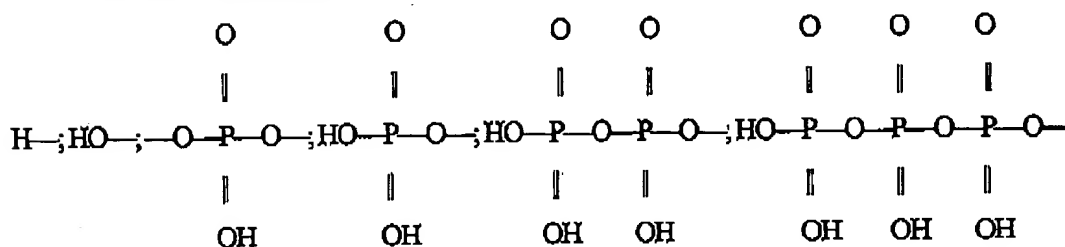
wherein A comprises at least three carbon atoms and represents at least one component of a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing directly or indirectly a detectable signal; and

wherein B and A are covalently attached directly or through a linkage group, and

wherein x comprises:



wherein y comprises:



wherein z comprises

H- and HO-

(ii)

Sig

|

PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 116 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety,

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal; and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

(E) transferring or subjecting said labeled fragments to a sequencing gel;

(F) separating or resolving said labeled fragments; and

(G) detecting directly or indirectly the presence of said labeled fragments by means of a metal or metal ion chelated by said chelating structure or chelating components.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

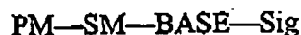
Page 117 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1705 (PREVIOUSLY PRESENTED) A process for detecting a nucleic acid of interest in a sample, which process comprises:

- (a) providing a sample which may comprise a nucleic acid of interest;
- (b) providing a metal or metal ion;
- (c) specifically hybridizing said nucleic acid of interest in the sample with one or more oligo- or polynucleotides, each such oligo- or polynucleotide being complementary to or capable of hybridizing with said nucleic acid of interest or a portion thereof, wherein said oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety; and

Sig is a signalling moiety comprising a chelating structure or component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety and at a position other than the C7 position when BASE is a 7-

Enz-5(D8)(C2)

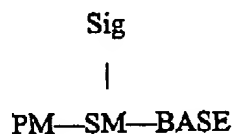
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 118 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

deazapurine moiety, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

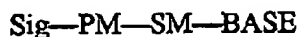
PM is a phosphate moiety ,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or component capable of providing chelating said metal or metal ion and a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety ,

SM is a furanosyl moiety,

BASE is a base moiety, and

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 119 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Sig is a signalling moiety comprising a chelating structure or components capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, and such covalent attachment does not substantially interfere with double helix formation or nucleic acid hybridization;

provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2', 3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and

(d) detecting the presence of Sig in any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest by means of said metal or metal ion chelated by said chelating structure or chelating components.

Claim 1706 (PREVIOUSLY PRESENTED) A process for detecting a nucleic acid of interest in a sample, which process comprises:

(A) providing:

(i) an oligo- or polynucleotide having two segments:

(a) a first segment complementary to and capable of hybridizing to a portion of said nucleic acid of interest; and

(b) a second segment comprising at least one protein binding sequence;
and

(ii) a metal or metal ion;

(iii) a detectable protein capable of binding to said protein binding sequence and comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal;

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 120 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

(B) contacting a sample suspected of containing said nucleic acid of interest with said oligo- or polynucleotide and said detectable protein (ii) to form a complex;

(C) detecting the presence of said protein in said complex and said nucleic acid of interest by means of said metal or metal ion chelated by said chelating structure or chelating component.

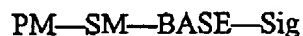
Claim 1707. (PREVIOUSLY PRESENTED) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising:

providing a cell;

providing a metal or metal ion;

contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable non-radioactive modified or labeled nucleotides or detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

(i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Enz-5(D8)(C2)

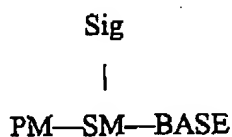
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 121 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

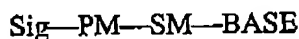
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

- (iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 122 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides by means of said metal or metal ion chelated by said chelating structure or chelating component, and determining the number of copies of said particular chromosome;

comparing said determined number of copies of said particular chromosome with a number of copies of said particular chromosome determined for a normal cell containing said particular chromosome; and

determining whether the number of copies of said particular chromosome in said cell is abnormal.

Claim 1708 (PREVIOUSLY PRESENTED) A process for identifying a chromosome of interest in a cell containing other chromosomes, the process comprising:

providing a cell;

providing a metal or metal ion;

providing a set of clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in said chromosome of interest, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 123 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

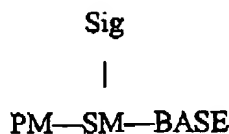
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Enz-5(D8)(C2)

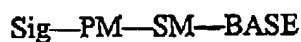
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 124 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said set of clones or DNA fragments or oligo- or polynucleotides, permitting specific hybridization of said set of clones or DNA fragments or oligo- or polynucleotides to said locus or loci in said chromosome of interest;

detecting by means of said metal or metal ion chelated by said chelating structure or chelating component any signal generated by each of said clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to said locus or loci in said chromosome of interest, and obtaining a pattern of hybridizations between said set of clones or DNA fragments or oligo- or polynucleotides and said chromosomes; and

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 125 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
— September 19, 2005]

identifying said chromosome of interest by means of said hybridization pattern obtained.

Claim 1709 (PREVIOUSLY PRESENTED) A process for identifying a plurality or all of the chromosomes in a cell of interest, the process comprising:

providing a cell of interest;
providing a metal or metal ion;
providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically hybridizable to a locus or loci in a chromosome of said cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs capable of detection, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA and wherein each set comprises a different indicator molecule, and wherein said modified or labeled nucleotide or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising:

(i) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is

Enz-5(D8)(C2)

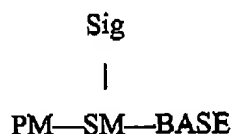
Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 126 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

a pyrimidine, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

(ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 127 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

— September 19, 2005]

least three carbon atoms, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

fixing the chromosomes from or in said cell;

contacting said fixed chromosomes under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to the locus or loci in said chromosomes; and

detecting by means of said metal or metal ion chelated by said chelating structure or chelating component any signal generated by each of said different indicator moieties in said sets of clones or DNA fragments or oligo- or polynucleotides which have specifically hybridized to the locus or loci in said chromosomes, and identifying a plurality or all of the chromosomes in said cell of interest.

Claim 1710 (PREVIOUSLY PRESENTED) A process for determining the number of chromosomes in an interphase cell of interest, the process comprising:

providing an interphase cell of interest;

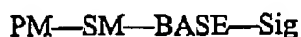
providing a metal or metal ion;

providing sets of clones or DNA fragments, or oligo- or polynucleotides derived from said clones, wherein each of said set of clones or DNA fragments or oligo- or polynucleotides are specifically complementary to or specifically hybridizable with at least one locus or loci in a chromosome of said interphase cell of interest, wherein each of said clones or DNA fragments or oligo- or polynucleotides in said sets comprise one or more detectable modified or labeled nucleotides or detectable modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotide or modified or labeled nucleotide analog comprise a nucleotide structure or nucleotide analog structure comprising:

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 128 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

- (i) a nucleotide structure or nucleotide analog structure having the formula



wherein

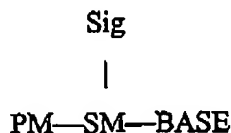
PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine, and at a position other than the C7 position when BASE is a 7-deazapurine;

- (ii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

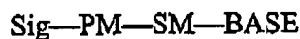
Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 129 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
— September 19, 2005]

attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii) a nucleotide structure or nucleotide analog structure having the formula



wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group;

contacting said interphase cell under hybridizing conditions with said sets of clones or DNA fragments or oligo- or polynucleotides, and permitting specific hybridization of said sets of clones or DNA fragments or oligo- or polynucleotides to any of the locus or loci in said chromosomes; and

detecting by means of said metal or metal ion chelated by said chelating structure or chelating component any signals generated by each of said sets of clones or DNA fragments or oligo- or polynucleotides specifically hybridized to the locus or loci in said chromosomes, to obtain a pattern of generated signals; and comparing each generated signal with other generate signals in said pattern, and determining the number of chromosomes in said interphase cell of interest.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 130 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1711 (PREVIOUSLY PRESENTED) A process for preparing a labeled oligo- or polynucleotide of interest, comprising:

(A) providing a metal or metal ion;

(B) providing:

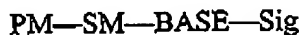
(1) one or more detectable chemically modified or labeled nucleotides or detectable chemically modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA or an oligo- or polynucleotide of interest, alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, wherein said other modified or unmodified nucleic acids are capable of incorporating into an oligo- or polynucleotide of interest, and wherein said modified or labeled nucleotides or nucleotide analogs comprise one or more signalling moieties comprising a chelating structure or chelating component capable of chelating a metal or metal ion and providing a detectable signal,

(2) an oligo- or polynucleotide comprising one or more of said modified or labeled nucleotides or modified or labeled nucleotide analogs (1), alone or in conjunction with one or more other modified or unmodified nucleic acids selected from the group consisting of nucleotides, oligonucleotides and polynucleotides, or

(3) both (1) and (2).

wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs (1) are modified on the furanosyl moiety, the phosphate moiety, the base moiety or any combination thereof, and wherein the modified or labeled nucleotides or modified or labeled nucleotide analogs comprise a nucleotide structure or nucleotide analog structure comprising :

(i)



wherein

PM is a phosphate moiety,

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
 Page 131 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
 (Following The September 8, 2005 Advisory Action)
 - September 19, 2005]

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal, wherein Sig comprises at least three carbon atoms, and

wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE directly or through a linkage group at a position other than the C5 position when BASE is a pyrimidine moiety, at a position other than the C8 position when BASE is a purine moiety, and at a position other than the C7 position when BASE is a 7-deazapurine moiety;

(ii)

Sig

|

PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a signal, wherein Sig comprises at least three carbon atoms, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; or

(iii)

Sig—PM—SM—BASE

wherein

PM is a phosphate moiety,

SM is a furanosyl moiety,

BASE is a pyrimidine, a purine or a 7-deazapurine base moiety, and

Sig is a signalling moiety comprising a chelating structure or chelating component capable of chelating said metal or metal ion and providing a detectable signal; wherein Sig comprises at

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 132 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

least three carbon atoms, and wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, provided that when said nucleotide or nucleotide analog structure (iii) is attached to an oligoribonucleotide or a polyribonucleotide, and provided that when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide; and said oligo- or polynucleotide of interest; and
(C) either incorporating said modified or labeled nucleotides or modified or labeled nucleotide analogs (A)(1) into said oligo- or polynucleotide, and preparing a labeled oligo- or polynucleotide of interest, or preparing said oligo- or polynucleotide of interest from said oligo- or polynucleotide recited in step (A)(2) above.

Claim 1712 (PREVIOUSLY PRESENTED) A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing a sample which may contain a nucleic acid of interest;
providing or generating (i) one or more detectable non-radioactively labeled oligonucleotides or polynucleotides, each of said detectable non-radioactively labeled oligonucleotides or polynucleotides comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest;
forming in liquid phase hybrids comprising said detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest;
separating or resolving in a gel said formed hybrids; and
detecting non-radioactively the separated or resolved hybrids to detect the presence of said nucleic acid of interest.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 133 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1713 (PREVIOUSLY PRESENTED) The process according to claim 1712, further comprising after said hybrid forming step, the step of subjecting the liquid phase to nuclease treatment.

Claim 1714 (PREVIOUSLY PRESENTED) The process according to claim 1712, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1715 (PREVIOUSLY PRESENTED) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprises DNA, RNA or DNA-RNA.

Claim 1716 (PREVIOUSLY PRESENTED) The process according to claim 1712, wherein said one or more detectable oligonucleotides or polynucleotides comprise biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or a combination of any of the foregoing.

Claim 1717 (PREVIOUSLY PRESENTED) The process according to claim 1712, wherein said non-radioactive detection step is carried out directly or indirectly.

Claim 1718 (PREVIOUSLY PRESENTED) The process according to claim 1712, wherein said detecting step is carried out by means of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1719 (PREVIOUSLY PRESENTED) The process according to claim 569, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1720 (PREVIOUSLY PRESENTED) The process according to claim 721, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 134 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1721 (PREVIOUSLY PRESENTED) The process according to claim 873, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1722 (PREVIOUSLY PRESENTED) The process according to claim 1025, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claims 1723-1724 (CANCELED).

Claims 1725-1726 (CANCELED).

Claim 1727 (PREVIOUSLY PRESENTED) The process according to claim 1712, wherein said detecting step comprises localizing said separated or resolved hybrids.

Claim 1728 (PREVIOUSLY PRESENTED) The process of any of claims 1700, 1701, 1702 or 1704, wherein in said providing step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1729 (PREVIOUSLY PRESENTED) The process of claim 1703, wherein in said detecting step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1730 (PREVIOUSLY PRESENTED) The process of claim 1705, wherein in said specific hybridizing step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1731 (PREVIOUSLY PRESENTED) The process of claim 1707, wherein in said contacting step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 135 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1732 (PREVIOUSLY PRESENTED) The process of any of claims 1700, 1701, 1702, 1703 or 1704, wherein said detecting step is carried out by a structure or component that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1733 (PREVIOUSLY PRESENTED) The process of any of claims 1700, 1701, 1702, 1703 or 1704, wherein in said detecting step, the chelating structure or chelating components have chelated said metal or metal ion comprising heavy metals, rare earth metals, or both.

Claim 1734 (PREVIOUSLY PRESENTED) The process of claim 1733, wherein said heavy metal comprises cobalt.

Claim 1735 (PREVIOUSLY PRESENTED) The process of claim 1732, wherein said detecting step is carried out radioactively.

Claim 1736 (PREVIOUSLY PRESENTED) The process of claim 1735, wherein said radioactive detection is carried out by means of an isotope.

Claim 1737 (PREVIOUSLY PRESENTED) The process of claim 1736, wherein said isotope is a β or γ emitter.

Claim 1738 (PREVIOUSLY PRESENTED) The process of claim 1735, wherein said radioactive detection is carried out with an isotope comprising bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 or yttrium-90.

Claim 1739 (PREVIOUSLY PRESENTED) The process of any of claims 638, 790, 942, or 1094, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

Claims 1740-1741 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 136 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1742 (PREVIOUSLY PRESENTED) The process of any of claims 887 or 1039, wherein said primers or said nucleoside triphosphates are labeled.

Claim 1743 (PREVIOUSLY PRESENTED) The process of any of claims 569, 721, 873, 1025, 1177, 1700, 1701, 1702, 1703 or 1704, wherein said base is a pyrimidine analog or a purine analog.

Claim 1744 (PREVIOUSLY PRESENTED) The process of claim 1743, wherein said pyrimidine analogs comprise thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs and deoxycytidine analogs.

Claim 1745 (PREVIOUSLY PRESENTED) The process of claim 1744, wherein said uridine analog comprises 5-bromo-2'-deoxyuridine-5'-phosphate.

Claim 1746 (PREVIOUSLY PRESENTED) The process of claim 1744, wherein said deoxycytidine analog comprises 5-hydroxymethyl-2'-deoxycytidylic acid.

Claim 1747 (PREVIOUSLY PRESENTED) The process of claim 1743, wherein said purine analogs comprise adenosine analogs, deoxyadenosine analogs, guanosine analogs or deoxyguanosine analogs.

Claim 1748 (PREVIOUSLY PRESENTED) The process of claim 1747, wherein said adenosine analogs comprise tubercidin or toyocamycin.

Claim 1749 (PREVIOUSLY PRESENTED) The process of any of claims 1706, 1708, 1709, 1710 or 1711, wherein in said providing step, the chelating structure or chelating components provide a detectable signal that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 137 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1750 (PREVIOUSLY PRESENTED) The process of any of claims 1705, 1706, 1707, 1708, 1709 or 1710, wherein said detecting step is carried out by a structure or component that is radioactive, fluorogenic, fluorescent, chemiluminescent, electron dense or magnetic.

Claim 1751 (PREVIOUSLY PRESENTED) The process of any of claims 1705, 1706, 1707, 1708, 1709, or 1710, wherein in said detecting step, the chelating structure or chelating components have a chelated metal or metal ion comprising heavy metals or rare earth metals.

Claim 1752 (PREVIOUSLY PRESENTED) The process of claim 1751, wherein said heavy metal comprises cobalt.

Claim 1753 (PREVIOUSLY PRESENTED) The process of claim 1750, wherein said detecting step is carried out radioactively.

Claim 1754 (PREVIOUSLY PRESENTED) The process of claim 1753, wherein said radioactive detection is carried out by means of an isotope.

Claim 1755 (PREVIOUSLY PRESENTED) The process of claim 1754, wherein said isotope is a β or γ emitter.

Claim 1756 (PREVIOUSLY PRESENTED) The process of claim 1753, wherein said radioactive detection is carried out with an isotope comprising bismuth-206, bismuth-207, cobalt-60, gadolinium-153, strontium-90 or yttrium-90.

Claim 1757 (PREVIOUSLY PRESENTED) The process of any of claims 1450, 1452, 1512, or 1514, wherein said fluorescent aromatic or cycloaliphatic group comprises a fluorescent dye.

Claims 1758-1759 (CANCELED).

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 138 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1760 (PREVIOUSLY PRESENTED) The process of any of claims 1473, 1474, 1475, 1476, 1705, 1707, 1708, 1709, 1710, or 1711, wherein said base comprises a pyrimidine analog or a purine analog.

Claim 1761 (PREVIOUSLY PRESENTED) The process of claim 1760, wherein said pyrimidine analogs comprise thymidine analogs, uridine analogs, deoxyuridine analogs, cytidine analogs or deoxycytidine analogs.

Claim 1762 (PREVIOUSLY PRESENTED) The process of claim 1761, wherein said uridine analogs comprise 5-bromo-2'-deoxyuridine-5'-phosphate.

Claim 1763 (PREVIOUSLY PRESENTED) The process of claim 1761, wherein said deoxycytidine analogs comprise 5-hydroxymethyl-2'-deoxycytidylic acid.

Claim 1764 (PREVIOUSLY PRESENTED) The process of claim 1760, wherein said purine analog comprises adenosine analogs, deoxyadenosine analogs, guanosine analogs or deoxyguanosine analogs.

Claim 1765 (PREVIOUSLY PRESENTED) The process of claim 1764, wherein said adenosine analogs comprise tubercidin or toyocamycin.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 139 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1766 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing at least one nucleic acid of interest;

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof, wherein each of said fragments comprises one or more detectable non-radioactively modified or labeled nucleotides;

subjecting said detectable labeled fragments to a sequencing gel to separate or resolve said fragments;

detecting non-radioactively the presence of said separated or resolved fragments by detecting the non-radioactively modified or labeled nucleotides; and

determining the sequence of said nucleic acid of interest.

Claim 1767 (PREVIOUSLY PRESENTED) A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments, wherein each of said fragments comprises one or more nucleotides, and wherein said one or more nucleotides comprise one or more fluorescent or chemiluminescent indicators on the furanosyl moiety, the phosphate moiety or the base moiety or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;

and

detecting non-radioactively said separated or resolved fragments by detecting the fluorescent or chemiluminescent indicators.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 140 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1768 (PREVIOUSLY PRESENTED) A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides that may be attached to, or coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent indicators are covalently attached, directly or through a linkage group, to the furanosyl moiety, the phosphate moiety, the base moiety of said nucleotides, or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;
and

detecting non-radioactively said separated or resolved fragments by means of said fluorescent indicators attached to said nucleotides.

Claims 1769-1773 (CANCELED).

Claim 1774 (CANCELED).

Claim 1775 (CANCELED).

Claim 1776 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest, comprising:

providing at least one nucleic acid of interest;

providing or generating detectable non-radioactively labeled nucleic acid fragments, each fragment comprising a sequence complementary to said nucleic acid of interest or to a portion thereof;

subjecting said detectable non-radioactively labeled fragments to a sequencing gel to separate or resolve said fragments;

detecting non-radioactively the presence of said separated or resolved fragments; and
determining the sequence of said nucleic acid of interest.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 141 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
- September 19, 2005]

Claim 1777 (PREVIOUSLY PRESENTED) A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:
providing or generating detectable non-radioactively labeled nucleic acid fragments;
subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;
and
detecting non-radioactively said separated or resolved fragments.

Claim 1778 (PREVIOUSLY PRESENTED) A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:
providing or generating detectable non-radioactively labeled nucleic acid fragments,
wherein said fragments comprise one or more detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, or the base moiety or any combination thereof;
subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;
and
detecting non-radioactively said separated or resolved fragments by detecting said modified or labeled nucleotides or said modified or labeled nucleotide analogs.

Claim 1779 (PREVIOUSLY PRESENTED) A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:
providing or generating detectable non-radioactively labeled nucleic acid fragments,
wherein said fragments comprise one or more detectable non-radioactively modified or labeled nucleotides or modified or labeled nucleotide analogs;
subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;
and
detecting non-radioactively said separated or resolved fragments by detecting said modified or labeled nucleotides or said modified or labeled nucleotide analogs.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 142 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

– September 19, 2005]

Claim 1780 (PREVIOUSLY PRESENTED) A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more detectable non-radioactive modified or labeled nucleotides or modified or labeled nucleotide analogs;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;
and

detecting non-radioactively said separated or resolved fragments by means of said modified or labeled nucleotides or said modified or labeled nucleotide analogs.

Claim 1781 (PREVIOUSLY PRESENTED) A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more detectable non-radioactive modified or labeled nucleotides or one or more detectable non-radioactive modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or modified or labeled nucleotide analogs have been modified or labeled on the furanosyl moiety, the phosphate moiety, or the base moiety or any combination thereof;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments;
and

detecting non-radioactively said separated or resolved fragments by means of the modified or labeled nucleotides or modified or labeled nucleotide analogs.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)
Page 143 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)
– September 19, 2005]

Claim 1782 (PREVIOUSLY PRESENTED) A process for detecting non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments, wherein each of said fragments comprises one or more nucleotides, and wherein said one or more nucleotides comprise one or more fluorescent indicators;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by detecting the fluorescent indicators.

Claim 1783 (PREVIOUSLY PRESENTED) A process for resolving or separating non-radioactively labeled nucleic acid fragments with a sequencing gel, comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising one or more nucleotides that can be attached to, or coupled to, or incorporated into DNA or RNA, and wherein one or more fluorescent indicators are covalently attached, directly or through a linkage group, to said one or more nucleotides;

subjecting said labeled fragments to a sequencing gel to separate or resolve said fragments; and

detecting non-radioactively said separated or resolved fragments by means of said fluorescent indicators attached to said one or more nucleotides.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 144 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116
(Following The September 8, 2005 Advisory Action)

— September 19, 2005]

Claim 1784 (PREVIOUSLY PRESENTED) A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing or generating (i) one or more detectable non-radioactively labeled oligonucleotide or polynucleotide, each of said detectable non-radioactively labeled oligonucleotide or polynucleotide comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotides or polynucleotides comprise one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to, coupled to, or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest;

forming liquid phase hybrids comprising said detectable non-radioactively labeled oligonucleotides or polynucleotides specifically hybridized with said nucleic acid of interest;

subjecting said liquid phase to nuclease treatment; and

detecting the hybrids non-radioactively to detect the presence of said nucleic acid of interest.

1785. (PREVIOUSLY PRESENTED) A process for detecting the presence of a nucleic acid of interest in a sample, comprising:

providing or generating (i) a detectable non-radioactively labeled oligonucleotide or polynucleotide, said detectable non-radioactively labeled oligonucleotide or polynucleotide comprising a sequence sufficiently complementary to said nucleic acid of interest or to a portion thereof to specifically hybridize therewith, wherein said detectable non-radioactively labeled oligonucleotide or polynucleotide comprises one or more detectable non-radioactively modified or labeled nucleotides or detectable non-radioactively modified or labeled nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and (ii) a sample that may contain said nucleic acid of interest; and

detecting hybrids non-radioactively to detect the presence of said nucleic acid of interest.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 145 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1786. (PREVIOUSLY PRESENTED) The process according to claim 1785, further comprising a treatment that acts upon a non-hybridized detectable non-radioactively labeled oligonucleotide or polynucleotide and leaves a hybridized detectable non-radioactively labeled oligonucleotide or polynucleotide intact.

Claim 1787. (PREVIOUSLY PRESENTED) The process according to claim 1786 wherein said treatment is a nuclease treatment.

Claim 1788. (PREVIOUSLY PRESENTED) The process according to claim 1784 or 1787 wherein said nuclease treatment is carried out by S1 nuclease, Exonuclease I from *E.coli*, or a combination thereof.

Claim 1789. (PREVIOUSLY PRESENTED) The process according to any of claims 1784, 1785, 1786 or 1787 further comprising separating or resolving in a gel said formed hybrids.

Claim 1790 (PREVIOUSLY PRESENTED) The process according to claim 1784 or 1785, wherein said nucleic acid of interest comprises DNA, RNA or DNA-RNA.

Claim 1791 (PREVIOUSLY PRESENTED) The process according to claim 1784 or 1785, wherein said detectable oligonucleotide or polynucleotide comprises DNA, RNA or DNA-RNA.

Claim 1792 (PREVIOUSLY PRESENTED) The process according to claim 1784 or 1785, wherein said detectable oligonucleotide or polynucleotide comprises biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten, an antibody component, a chelating component or a combination of any of the foregoing.

Claim 1793 (PREVIOUSLY PRESENTED) The process according to claim 1784 or 1785, wherein said non-radioactive detection step is carried out directly or indirectly.

Enz-5(D8)(C2)

Dean L. Engelhardt et al., Serial No.: 08/486,069 (Filed: June 7, 1995)

Page 146 [Supplemental Amendment To Applicants' July 7, 2005 Amendment Under 37 C.F.R. §1.116 (Following The September 8, 2005 Advisory Action)

- September 19, 2005]

Claim 1794 (PREVIOUSLY PRESENTED) The process according to claim 1784 or 1785, wherein said detecting step is carried out by means of an enzymatic measurement, a fluorescent measurement, a chemiluminescent measurement, a microscopic measurement or an electron density measurement.

Claim 1795 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising: (a) a sequence complementary to said nucleic acid of interest or a portion thereof, and (b) fluorescent labels covalently attached, directly or through a linkage group, to said fragments;

subjecting said labeled fragments to a sequencing gel to separate or resolve said labeled fragments;

detecting non-radioactively said separated or resolved fragments by means of said attached fluorescent labels; and

determining the sequence of said nucleic acid of interest from said detected fragments.

Claim 1796 (PREVIOUSLY PRESENTED) A process for determining the sequence of a nucleic acid of interest comprising:

providing or generating detectable non-radioactively labeled nucleic acid fragments comprising: (a) a sequence complementary to said nucleic acid of interest or a portion thereof, and (b) different fluorescent labels covalently attached, directly or through a linkage group, to said fragments;

subjecting said labeled fragments to a sequencing gel to separate or resolve said labeled fragments;

detecting non-radioactively said separated or resolved fragments by means of said attached different fluorescent labels; and

determining the sequence of said nucleic acid of interest from said detected fragments.

* * * * *

Enz-5(D8)(C2)